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SEGMENTAL OCCLUSION OF MAJOR ARTERIES*

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THE SPECIALTY of vascular surgery has made rapid strides in the past four years because of the introduction of practical methods of replacing or by-passing non-functioning diseased arterial segments. These techniques have been made possible by the use of grafts, which may consist of homologous artery, autogenous vein or plastic cloth tube. It is our purpose in this presentation to review these methods and, on the basis of our experience, to present what we believe are the best techniques available at present.

The first point to be emphasized is that of case selection. Grafting procedures should not be used without well-defined indications or the percentage of successes will drop markedly. Table I indicates the type of case in which investigation may reveal possibilities for improving the circulation to the ischæmic limb. Arteriosclerosis obliterans is the pathological process underlying the great majority of cases. Table II illustrates the criteria necessary before a grafting procedure should be considered. We have been increasingly surprised at the number of cases of arterial ischæmia to the leg which have been shown to be segmental in type. The more arteriography is used, the more cases suitable for surgery will be discovered. One can routinely expect to find segmental occlusion in the person with intermittent claudication and what appears to be a relatively normal foot, but one is surprised to see segmental blockage in others with acute gangrene or pre-gangrene of toes or part of the foot after slow or acute thrombosis and neglected embolism. We have been successful in revascularizing 12 limbs where previously a major amputation would likely have been the final result. This does not mean that we have succeeded in re-establishing pedal pulses in all cases. Frequently an iliac segmental occlusion will be associated with occlusion in the anterior and posterior tibial arteries. However, by increasing the main vessel flow down to the knee level, the collateral supply to the foot is so greatly improved that the desired clinical result is achieved.

TABLE I.

TYPES OF CASES WHERE GRAFTING MAY BE INDICATED

1. Arterial aneurysms, the majority occurring below the level of the renal arteries.
2. Intermittent claudication with no great degree of trophic ischæmic changes in the feet.
3. Relatively recent episodes of arterial thrombosis which have little or minor degree of distal gangrene.
4. More extensive gangrene which reveals a good line of demarcation in the weeks subsequent to onset.

TABLE II.

CRITERIA FOR SELECTION OF CASES

1. Good quality femoral or aortic arteriograms.
2. Evidence that the arteriosclerotic process is not severely widespread in the arteries under consideration.
3. Evidence that the outflow distal to the occluded segment is of good calibre.
4. No major arteriosclerotic manifestations in cerebral, cardiac or renal areas.
5. Availability to an arterial bank or, as second choice, the use of plastic cloth prostheses.
6. Plenty of operating time, a steady hand and an equable temper.

TECHNIQUES

1. *Grafts:*

The surgeon is aware of the many methods of collecting and storing arterial homografts and probably wonders which he should adopt. First of all, good rapport must exist between the

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surgeon and the pathologist because the latter is the kingpin of the arterial bank. He hates to have an autopsy delayed while the surgeon or his house staff gets there with the complete sterile set-up necessary for taking a sterile graft. The surgeon may be busy or unavailable when a suitable autopsy is available and a changing house staff cannot always be counted on to take a graft without contamination. We have wasted many a graft through such contamination.

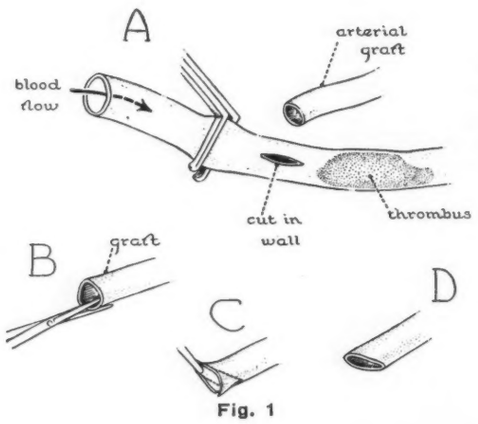

Fig. 1

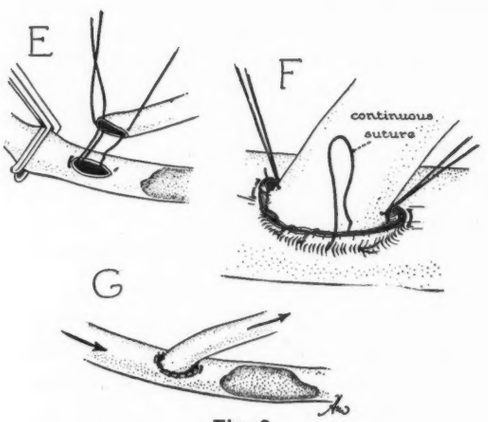

Fig. 2

In consequence of these tribulations we have adopted the technique described by the Ford Hospital group in Detroit, where the arteries for the bank are taken by the pathologist during regular autopsy. They are kept in Ringer's solution and treated by our biochemist the following day with beta propiolactone, which sterilizes the graft chemically without obvious harm. The sterilized grafts are kept in nutrient solution at 4° C. for three weeks, and if not used by that time are freeze-dried for long-term storage. We have also enlarged the scope of eligible donors. If the body has not been cooled, the grafts should be taken before six hours. If cooled, double this period is acceptable. Cancer, as in brain tumours, is not a contraindication and material from those dying of acute infections is also acceptable. After 50 years of age the majority of people's vessels show sufficient sclerosis to make them unsuitable as donors.

2. *Types of Grafts:*

Venous autografts are useful and we still employ these in the occasional case where a suitable homograft is not available. However, they have distinct limitations, as they cannot safely be employed to replace vessels larger than the superficial femoral because the flow in major vessels produces too great a dilatation of the vein graft. The vein selected should be originally smaller than the artery to be replaced because of this dilatation. Use of the saphenous vein to replace the superficial femoral artery gives a good idea of the proportional sizes. When a saphenous autograft is being cut, the vein goes into marked spasm and overcoming this spasm complicates the procedure. Also the smaller calibre of the vein makes the technique of anastomosis more difficult, with a consequent increased rate of graft failure. These points are all obviated by the use of an appropriate homograft.

In the past two years the use of fine-mesh plastic cloth as an arterial graft has received considerable attention. Orlon, dacron, nylon and vinyon N. have been employed. Enough clinical and experimental data are now available to indicate that these do work, but only with relative certainty in major vessels such as the aorta. I am unable to give a personal opinion on their worth, but I can see no great hurry to change over to plastic prostheses if an adequate bank of arterial homografts is on hand. Cases with homografts implanted more than five years have been reported and it does not appear that degenerative changes in the homograft are going to be as dire as was originally predicted by some sceptics.

3. *Methods of Anastomosis:*

Until this year replacement of a segmentally occluded artery by a graft was accomplished by excision of the affected segment by an end-to-end anastomosis with the graft. This technique works well in arteries of major size (external iliac or larger) because an adequate lumen at

the site of anastomosis can be achieved. However, when an end-to-end junction must be made in the superficial femoral artery, especially as it gets toward the popliteal, the lumen is frequently stenosed to the point where some degree of stasis occurs in the graft and the likelihood of graft thrombosis is very probable. In the past three years we have in 34 cases performed excision and grafting by this technique, using autogenous vein grafts or homologous arterial grafts. Sixteen of these were in vessels of the calibre of the external iliac or larger and were all homografts, and I am happy to say that only one case of graft thrombosis occurred. In 18 cases the segmental occlusion was in the superficial femoral artery and I regret to state that graft thrombosis occurred either immediately or in the subsequent two months in 10 cases. These failures occurred about equally in autogenous vein and homologous arterial grafts. Not only is end-to-end anastomosis technically difficult in a vessel of small calibre but also the intima of the distal host artery shows marked thickening in all these cases of arteriosclerosis obliterans, further narrowing the anastomotic lumen. Excision with end-to-end suture also frequently damages good functioning collaterals, as the distal patent artery usually commences just at the point of a large incoming collateral vessel. Of our 10 failures in this type of anastomosis two subsequently required a major amputation.

Recently Linton of Boston, following the original idea of Kunlin, has advocated an improved anastomotic technique—that of the end-to-side by-pass graft. The occluded arterial segment is left undisturbed and is by-passed by a homograft attached to the host artery proximal and distal to the obstruction (Figs. 1 and 2). This is a big advance, as the suture technique is simpler, the size of the anastomotic opening can be made as large as the obliquely cut end of the graft will allow, and there is no danger of damaging functioning collaterals. Operating time is reduced, because dissection of the occluded artery is unnecessary. For the past four months all of our anastomoses have been by this technique, except in the proximal aorta. During this time, nine cases had this end-to-side by-pass technique performed, the longest graft being from the common iliac to the popliteal. All have been successful in giving return of distal pulses or clinical and oscillometric evidence of a marked improvement in distal blood flow. I feel that this is the method of the future and that many limbs will be saved if the selection criteria are closely observed.

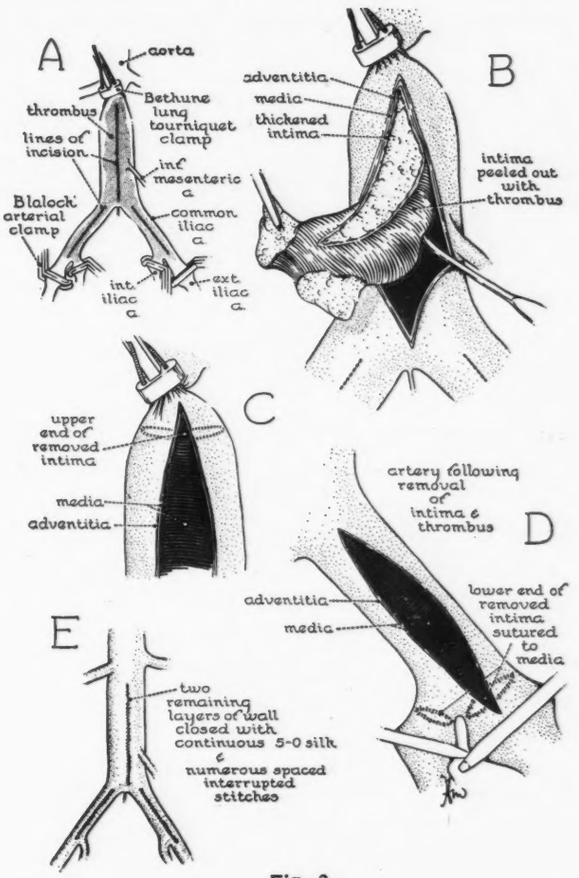

Fig. 3

4. *Thromboendarterectomy* (Fig. 3):

This technique of cleaning out the intima and occluding debris from the involved segment is still a useful procedure, although one has heard less of it in the past year, because of the greater availability of arterial grafts. It is an alternative to grafting and is technically simpler. It too will give spectacular results in the well-selected case. However, over-all results will not be as good as when grafts are used. An unsuspected calcified plaque involving the media may make the arterial wall so thin that repair is dangerous because of the risk of subsequent rupture or aneurysm formation. Also, it is difficult to tack down the distal cut end of the intima to prevent its stripping downward and folding in like a valve when blood flow is re-established in the intimectomized area. We used to do more of these operations when grafts were not so freely available, but still prefer this technique when a short segment of an artery is occluded in a

vessel of the calibre of the external iliac artery or larger.

In conclusion, may I emphasize again the surprisingly large number of cases of segmental arterial occlusion which exist. You will discover them by clinical suspicion with arteriographic proof. Employing the end-to-side technique with arterial homografts will result in the salvage of many limbs originally thought to be irretrievably damaged.

ON OSTEOCLASTOMA AND RELATED PROBLEMS

A SURVEY OF HONEYCOMB LESIONS OF BONE IN NOVA SCOTIA

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THE DIFFERENTIAL DIAGNOSIS of osteoclastoma has been radically altered in recent years by the work of Jaffe and Lichtenstein at the Hospital for Joint Diseases in New York. Their many communications have been brought together in a monograph by Lichtenstein (1952)[1] The original references have been consulted, but for convenience and unless otherwise stated, where Jaffe and Lichtenstein are cited the monograph is given as reference since it contains all relevant data. In this paper it is our purpose to review, in the light of the work of Jaffe and Lichtenstein, all osteoclastomas and all other conditions involved in the differential diagnosis which were encountered in the Province of Nova Scotia (population 656,000) in the five-year period September 1950 to August 1955. Old cases coming up for review during this period are also included.

The essence of the contributions of Jaffe and Lichtenstein to the problem of osteoclastoma is as follows. (1) The tumour is rare. (2) It is not likely to develop under the age of 20 years. (3) While some tumours are treated successfully by operation or irradiation, some are undoubtedly aggressive and prone to recur, and occasional ones behave like frank sarcomas. (4) While radiologically the tumours may be honeycomb, the emphasis is generally on lysis; in fact, a honeycomb is usually more pronounced in other conditions such as non-osteogenic fibroma, aneurysmal bone cyst, or chondromyxoid fibroma. (5) Since the osteoclastoma is a formidable tumour, it is important to recognize that it is not a radiological entity. (6) Care must be exercised in sharply distinguishing histologically other entities which simulate osteoclastoma. (7) In relation to this latter problem, Jaffe and Lichtenstein have described two new entities which are wholly benign—aneurysmal bone cyst and chondromyxoid fibroma. They have also made important contributions to our knowledge of other conditions related to the problem and have introduced new terms, which they consider clarify an otherwise confusing situation, namely, central xanthofibroma of bone (their non-osteogenic fibroma), localized osteitis fibrosa (their fibrous dysplasia) and the chondromatous giant cell tumour of Codman (their benign chondroblastoma). (8) It is emphasized that, in sharp contrast to osteoclastoma, not only are these entities wholly benign but they are mainly encountered in patients under 20, and usually in childhood and adolescence, while their sites of predilection are different from those of osteoclastoma. (9) They doubt whether treatment by irradiation is useful.

Thus from the work of Jaffe and Lichtenstein there have evolved the following highly practical broad rules. In childhood and adolescence, a variety of simple tumours and dysplasias are encountered as single honeycomb lesions and are widely distributed over the skeleton. On the other hand, the osteoclastoma is a formidable lesion, is rarely encountered under the age of 20, and apart from the jaw is confined to the ends of long bones and almost entirely to the lower end of the femur, the upper end of the tibia, the distal end of the radius and occasionally the upper end of the humerus.

It may be stated from the outset that there is one departure from the teaching of Jaffe and Lichtenstein. Jaffe, Lichtenstein and Portis[2] are quite rigid in their definition of classical osteoclastoma. Pathologists will agree with this. Morphologically the classical osteoclastoma includes, in addition to areas containing spindle cells and giant cells, areas of interlacing bundles of fibrocellular tissue in which there may be few giant cells or none. These workers, however, contend

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that osteoclastomas arise from marrow cells while, I think correctly, Willis[3] takes the view that osteoclastomas arise from and consist of bone formative cells in which there is merely a strong bias to osteoclasis; I am in agreement with Shufstall and Gregory[4] that some areas of almost all examples show some formation of woven bone by the tumour cells (Fig. 1). This

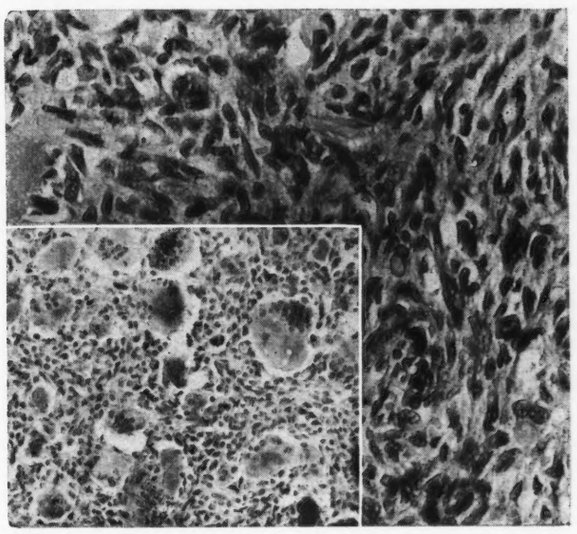

Fig. 1a.—Superimposed on Fig. 1b. 1a shows typical osteoclastoma; 1b from same tumour shows fibrocellular tissue with woven bone.

function is often greatly increased by irradiation of the tumour. In the mistaken belief that osteoclastoma does not arise from osteogenic tissue, Jaffe and Lichtenstein exclude all possibility of transition between osteoclastoma and other osteogenic tumours. I accept their analysis of the literature placing many alleged (xanthomatous, chondromatous and angiomatous) variants under what they now term chondromyxoid fibroma, benign chrondroblastoma, and non-osteogenic fibroma, and their careful exclusion of dysplasias including aneurysmal bone cyst. Apart from aneurysmal bone cyst, distinction for their new entities is, however, based on age of onset, site, and prognosis much more clearly than on basic histogenetic differences, and I consider that transitions between osteoclastoma and other osteogenic tumours also occur. Thus in my review I will cover the following: (1) highly malignant tumours behaving like osteogenic sarcomas but showing histogenetic relationship to osteoclastoma; (2) classical osteoclastoma; (3) variants of osteoclastoma and other simple osteogenic tumours; (4) the new entities described by Jaffe and Lichtenstein; (5) simple angioma of bone which occasionally may simulate osteoclastoma radiologically.

MALIGNANT OSTEOCLASTOMA

During the period of the survey I encountered two tumours which were much more atypical than the classical osteoclastoma and rapidly metastasized. They merely serve to show that within the limits of morphology one has to recognize transitions between osteogenic sarcoma and osteoclastoma.

CASE 1.—*Malignant osteoclastoma.* Mrs. M.M., aged 19; rapidly expanding lytic growth of upper end of left humerus. Treated by disarticulation. Death from pulmonary metastases within six months of first symptoms. The panel of the Canadian Tumour Registry agreed with the diagnosis of malignant osteoclastoma on examination of the operative specimen.

CASE 2.—*? Malignant osteoclastoma.* J.Y., male, aged 27; 10 weeks' history of pain and discomfort in pelvis followed by radiological finding of massive lysis and expansion of bony pelvis. Death from pulmonary metastases within six months of first examination. On examination of material from the primary tumour and metastases, the panel of the Canadian Tumour Registry were equally divided betwen a diagnosis of osteogenic sarcoma and malignant osteoclastoma.

CLASSICAL OSTEOCLASTOMA

The following two cases were the only examples encountered during the period of the survey.

CASE 3.—*Classical osteoclastoma.* W.C., male, aged 38; pain and stiffness and latterly swelling above left knee. Radiological examination: a lytic honeycomb tumour expanding the medial condyle. Biopsy: classical morphology of osteoclastoma. Treated by curettage and use of bone chips. Operative specimen had a similar morphology to biopsy specimen. Two years later, free from complaint and no radiological abnormality present.

CASE 4.—*Classical osteoclastoma.* Mrs. B.MacN., aged 34; pain and swelling of right knee of three months' duration. Radiological examination; a lytic honeycomb tumour expanding the upper end of the right tibia. Treated by curettage and use of bone chips. Material had classical morphology of osteoclastoma. Six months later free from complaint and no radiological evidence of recurrence.

Review Cases

During the period of the survey the following cases of osteoclastoma, previously treated, came up for review.

CASE 5.—*Successful conservative treatment of irradiation-resistant osteoclastoma.* Mrs. van der K., aged 37; June 1949, sustained a pathological fracture of lower end of left femur. Radiological examination: a lytic tumour expanding both condyles of femur. Biopsy: classical osteoclastoma. Treated by irradiation 1,512 r. October 1949, extension of lesion revealed by the late egg-shell clinical and radiological picture. Tumour curetted and

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packed with bone chips after cauterization with phenol. Plaster case applied from groin to ankle with knee in flexion. To date there has been no recurrence and the patient now has a useful limb. Examination of tumour: classical osteoclastoma.

CASE 6.—*Osteoclastoma followed by irradiation-induced sarcoma.* Miss M.H., June 1949, when almost 17, sustained a pathological fracture of lower end of left femur. Radiological examination: an osteolytic honeycomb lesion expanding both condyles. Biopsy: classical osteoclastoma. Treatment by irradiation 1,512 r. October 1949, radiological examination revealed further expansion of the lesion. Tumour excavated by curettage, cauterized with phenol and packed with bone chips. Histological examination of material: classical osteoclastoma in all serial sections. From the operation until June 1951, seen at seven review sessions with no evidence of clinical or radiological progression, but the questionable persistence of a radiolucent defect was noted. In August 1951 had pain and disability and a lytic defect. In December 1951, rapid progression of defect to complete destruction of both condyles and part of shaft. High amputation was performed. Examination of the specimen revealed a sarcoma composed of regularly interlacing bundles of fibrocellular collagen. Mitotic figures and markedly atypical nuclei were present but not numerous. In a few areas the collagenous stroma appeared to condense to produce woven bone. June 1952, pulmonary metastases identified radiologically. August 1952, patient died at home from pulmonary metastases. I can only regard the sarcoma as having been induced by the irradiation; all specimens have been thoroughly examined and reviewed.

Fig. 2.—Osteoclastoma of head of humerus (Case 7).

CASE 7.—*Osteoclastoma showing rapid progression and resistance to irradiation.* W.O'G., male, in 1947 when aged 22, sustained a pathological fracture of the head of the left humerus after complaining of a sore shoulder for one year. Radiological examination: a honeycomb lesion expanding the head of the left humerus (Fig. 2). Biopsy: classical osteoclastoma. Treatment was by irradiation, 3 sessions of ten days, 225 r on each day, in July and December 1948 and June 1949. During the period of treatment radiological examination revealed progressive growth to reach a volume more than twice the original, with extension down the shaft. There was the usual increased density in the scalloped margins of the honeycomb induced by the irradiation. Finally, in view of the ominous progression and large size, the tumour was removed by disarticulation. The histological appearance of the specimen was similar to that in the original biopsy with, in addition, many areas showing formation of woven bone by the tumour cells, no doubt, secondary to the stimulus of irradiation. The tumour had broken through its capsule and invaded muscle, indicating the correctness of the radical surgery. The patient has been followed up to date, with no evidence of metastases.

Comment

Lichtenstein (p. 98)[1] states that "on a fair-sized orthopædic hospital service, one is not likely to encounter more than two or three cases [of osteoclastoma] a year, on the average." My finding of only two classical cases, one highly malignant variant and one debatable variant, over a five-year period in a population of 656,000 stresses the rarity of the tumour. During this period three older cases came under review. My previous experience in Saskatchewan where I filtered the material from a population of half a million indicates that the incidence in those regions is of the order of one per million of population per year. It is considered that there is now general agreement that osteoclastoma covers a range of tumours from highly malignant tumours where there is debate whether to classify them as malignant osteoclastomas or as osteogenic sarcomas through undoubted malignant forms with metastases though usually there is a history covering some years before metastases occur, and locally malignant forms only curable by radical surgery to benign growths curable by curettage. Lichtenstein (p. 108)[1] considers that one-half are curable by conservative treatment, one-third will be more aggressive and many of them will require amputation, and the remainder are frankly malignant and prone to metastasize to the lungs.

Jaffe, Lichtenstein and Portis[2] consider that, within limits, the prognosis can be forecast by grading the tumours according to histological atypism, and they employ three grades. Willis[3] contends that this distinction is not possible on morphological criteria. Examination of my small series shows the highly malignant and the debatable example, as one would expect, to be even more anaplastic than they illustrate for the highest grade (grade three) while the others are all low-grade (grade one) except Case 6 of the review cases which is of grade two. In addition, I have previously studied a case of an osteo-

clastoma, grade one, of the lower end of the femur in a young woman of 21 where the original biopsy and amputation specimen showed universal invasion of veins in the surrounding muscle. The patient died from pulmonary metastases. Grading appears to be of limited value.

Jaffe and Lichtenstein are sceptical of the use of irradiation. This small survey suggests that irradiation may be a stimulant to growth in some cases and entails the hazard of the induction of sarcoma. Furthermore, persistence with treatment may lead to much mischief, as in Case 7 of the reviews where the surgeon was eventually left with a very large tumour which might have yielded to conservative operation had this been the initial treatment. The results leave the same implication as that given by Jaffe and Lichtenstein, namely, that the therapist's confidence in irradiation has persisted because of the mistaken inclusion of a variety of dysplasias and other simple tumours in their series.

The site of the tumours confirms the opinions of Jaffe and Lichtenstein, who insist that apart from the jaw the tumour is almost confined to the long bones. Lichtenstein (p. 98)[1] states, "I have observed only a single instance in an innominate bone, and have never experienced one in a rib, a clavicle, an ulna, or a bone of the calvarium."

VARIANT OF OSTEOCLASTOMA

Transition to ossifying fibroma.

In a mistaken belief that osteoclastoma does not arise from osteogenic tissue, Jaffe and Lichtenstein exclude all possibility of transition between osteoclastoma and other osteogenic tumours. Considering the age, site, radiological findings and morphology of the case to be described, I cannot place it under any classical entity and can only place it as a variant between osteoclastoma and osteogenic fibroma.

CASE 8.—L.McK., aged 42, male, had a painful swollen wrist for 10 months. Radiological examination revealed an expansion of the distal end of the radius, 3.5 cm. in diameter, with marked thinning of the cortex and showing a fine honeycomb reticulation with no sclerosis. This is a site of election for osteoclastoma and it was shown in conference by the radiologist as a classical example of osteoclastoma. The tumour was treated by curettage and bone chips and rapidly resolved. The tissue was firm and reddish with bright yellow pockets. Serial sections showed two-thirds of the tumour to be composed of typical fibroma with, as is common in such tumours in bone, the yellow pockets explained by xanthomatous change. The fibroma was not cellular, in contrast with the fibrocellular areas of osteoclastoma. The remainder of the tumour was accounted for by pockets of typical osteoclastoma and spicules and large islets of uncalcified woven bone not accounted for by organization of hæmorrhage. It is considered that the tumour is an osteoclastoma with much transition to ossifying fibroma and including xanthomatous change as is common in fibromas in bone. This tumour is most unlikely to inherit the dubious prognosis of osteoclastoma and it would be a mistake to classify it under osteoclastoma without reservations. Its inclusion, however, under osteoclastoma would not alter the rarity of these tumours. Some may wish to argue that the lesion is a dysplasia. The site and radiological appearances are against this. Whatever the truth, the argument is confined in its classification as benign and not as having the dubious prognosis of osteoclastoma.

CHONDROMYXOID FIBROMA

A distinctive neoplasm clearly separable from osteoclastoma.

CASE 9.—J.F., schoolgirl, aged 16, complained in April 1951 of a slight swelling of the right heel and aching pain of 18 months' duration. Clinical examination revealed slight soft tissue swelling over the right os calcis. Radiological examination revealed a small radiolucent defect in the inferior part of the os calcis. The lesion was considered to be tuberculous, and treated by immobilization in a plaster cast and chemotherapy. In July 1951, radiological investigation revealed marked extension of the osteolytic lesion. There were now four small draining sinuses over the area; *Staph. pyogenes* was obtained on cultures, and healing was rapid after penicillin therapy and compresses. Antituberculosis chemotherapy was continued. In October 1952, great pain

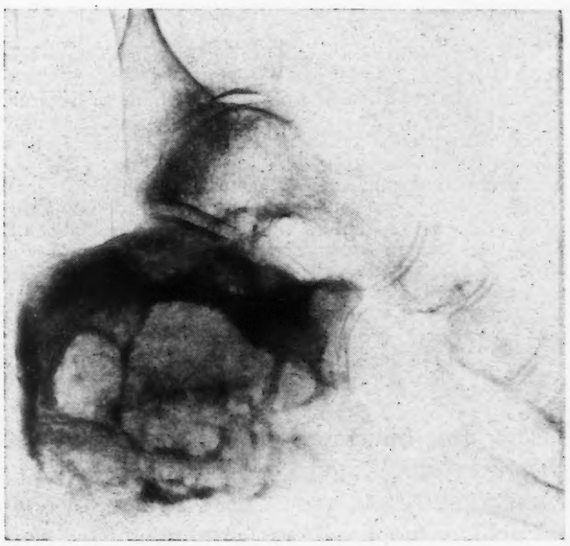

Fig. 3.—Chondromyxoid fibroma of os calcis (Case 9).

and disability was experienced and the lesion of os calcis was now extensive (Fig. 3). A biopsy specimen was obtained and reported as chondromyxoid fibroma, and attention was drawn to the literature. In view of the report, thorough curettage was carried out with removal of most of the interior of the os calcis. This yielded a reddish yellow and brown, moderately firm tissue. The expanded thin shell of cortical bone was packed with bone chips from the iliac crest of the patient. Healing progressed rapidly with solid incorporation of the bone

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Fig. 4.—Chondromyxoid fibroma showing mosaic of cells and matrix. × 20.

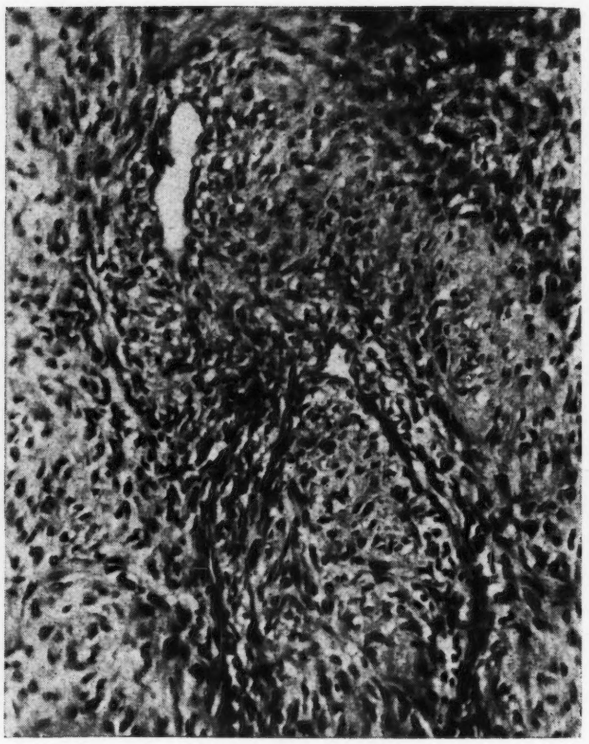

Fig. 5.—Chondromyxoid fibroma. × 180.

chips during the next six months. In December 1954, the os calcis was completely normal and the patient, now a nurse, had no symptoms despite much walking.

Pathological Report

This is a distinctive neoplasm: (1) It has everywhere a remarkably uniform mosaic structure (Fig. 4). (2) This is determined by trabeculæ containing well-formed large vascular channels cuffed by a delicate reticulum which embraces a loose tissue containing well-differentiated spindle-type connective tissue cells and occasional multinucleated giant cells. (3) This loose cellular tissue frays out as multiangular fibrocytes into a mucoid matrix broken up by fine collagenous fibrils in which one can rarely make out faint lacunæ containing large, rounded, pale cells indicating the essential link with cartilage (Fig. 5). Mitotic figures are very hard to find and bizarre nuclear forms are not a feature. In a few areas giant cells are conspicuous.

Comment

This case illustrates all of the features of a chondromyxoid fibroma as defined by Jaffe and Lichtenstein. It is a rare growth and the only example encountered by the author. The common site is a bone of the lower limb. Symptoms develop at an early stage of the lesion and though it has occasionally been observed in older patients most cases occur in adolescents or young adults. First symptoms in this case were noted when the patient was 14½. The regular mosaic architecture and regular histological features are quite distinctive and not to be confused with osteoclastoma, but the phase of rapid growth, lack of marked surrounding sclerosis and the histological picture could lead to a mistaken diagnosis of myxosarcoma or chondrosarcoma even though there is no calcification. The remarkable final healing despite the gross nature of the lesion indicates the essential benignity of the growth. Jaffe and Lichtenstein have performed an important service in defining this growth. If biopsy had been carried out with first symptoms when the growth was very small, the curettings, perhaps traumatized, would likely have been mistaken for myxosarcoma if the mind was not alerted to the characters of chondromyxoid fibroma.

Although it must be recognized as a distinctive clinico-pathological entity, no doubt the tumour is histogenetically related to the osteoclastoma.

ANEURYSMAL BONE CYST

Pritchard[5] has detailed the historical background leading to the separation of hyperparathyroidism, with its generalized osteoporosis as well as focal lesions, from localized osteitis fibrosa in which there are three chief features: (1) skeletal lesions affecting one, a few, or almost all bones in the body; (2) patchy pigmentation of the skin; (3) endocrine disturbances. The skin

and endocrine disturbances need not be present and indeed are rare. Lichtenstein and Jaffe[6] have introduced and popularized the term fibrous dysplasia for the skeletal lesions, monostotic and polyostotic. The lesion, as commonly encountered, is single and is found in childhood or adolescence. Bone is being constantly broken down and reconstructed. In fibrous dysplasia it is convenient to regard the affected area as having a local congenital defect so that the reconstruction becomes progressively defective, ultimately replacing normal bony structure with a less organized and less rigid tissue. This tissue commonly consists of interlacing bundles of fibrocellular connective tissue and, to a variable degree, other constituents of the bony mesenchyme (woven bone, irregular spicules of lamellar bone, cartilage, giant cells, variable vascularity).

The aneurysmal bone cyst was first described by Jaffe and Lichtenstein[7] and later described in detail separately by the same authors.[8, 9] Histologically the lesion is similar to fibrous dysplasia with the added remarkable development of large vascular channels which gives the condition its striking and distinctive clinico-pathological attributes. In view of its apparent "blowing up" after slight trauma, these authors and others believe that the lesion takes origin from a vascular accident possibly associated with an underlying vascular malformation, but in our present state of knowledge for all practical purposes it can be considered a variant of fibrous dysplasia. The distinctive feature of the condition is illustrated in the following two cases.

CASE 10.—*Aneurysmal bone cyst of scapula.* When L.J., a girl, was 5 years of age in 1950, she sustained a fracture of the right forearm after a fall. This healed without incident but about the same time she complained of pain behind the tip of the left shoulder and later a lump was noticed which was tender from the outset and increased in size. Clinical examination revealed a tender almost fluctuant swelling two inches in diameter medial to the acromion of the left scapula. All movements of the left shoulder were well carried out, but the tumour was extremely sensitive, producing pain on the slightest touch. Radiological examination revealed a multiloculated osteolytic lesion arising from the posterior surface of the scapula in the angle between the coracoid process and the superior wing of the scapula. At operation a cyst was exposed through the supraspinatus muscle which ruptured on probing and was found to be about two inches in diameter and filled with gelatinous clot. Apart from its base in the scapula it had a thin egg-shell covering. The cyst was partly excised. Six months later the patient, who had moved to another district, reported with complaints and findings as before; radiological examination showed a multiloculated radiolucent lesion of the scapula, scalloped and condensed on its inner margin (Fig. 6). This was completely excised. There was much bleeding at the operation.

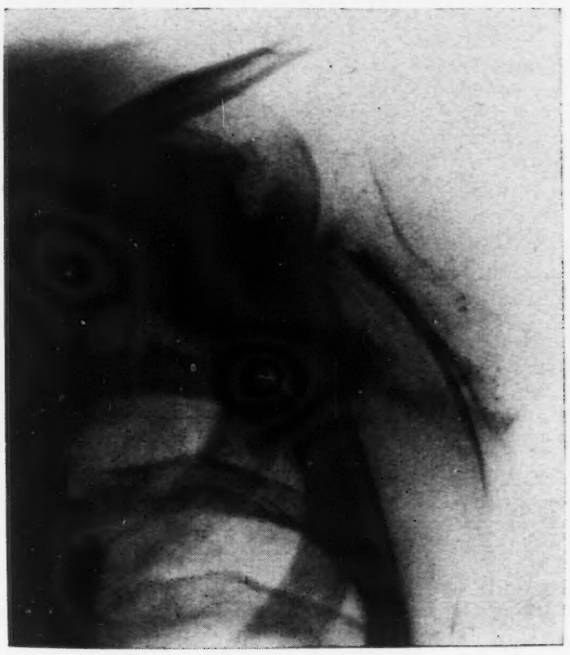

Fig. 6.—Aneurysmal bone cyst of scapula (Case 10).

Pathological Examination

The specimen consisted of a multilocular cyst in which large spaces were filled with blood. The cyst had a thin but well-defined capsule of fibrous tissue enclosing a thin, imperfect rim of bony lamellæ. On its outer aspect it merged with slight fibrosed muscle showing some lymphocytic infiltration. The trabeculæ forming the locules consisted of a well-differentiated fibrocellular tissue containing spindle cells and osteoclasts and often thin strands of woven bone. The trabeculæ enclosed large vascular channels lined by a single layer of endothelium resting on the cellular trabeculæ. Particularly where the large vascular channels had ruptured, the endothelial lining had disappeared and the blood lay in contact with the cellular stroma of the trabeculæ (Figs. 7 and 8).

The lesion was clearly similar histologically to fibrous dysplasia by virtue of the variety of osteogenic tissue but differed from classical fibrous dysplasia by virtue of the numerous large vascular channels. The tissue was sent as an example of dysplasia to the Canadian Tumour Registry. Material was forwarded to Dr. Lichtenstein and the diagnosis given was of aneurysmal bone cyst. My reaction, perhaps a common initial one to the contributions of Jaffe and Lichtenstein, was—why add yet another name to the pathology of dysplasia? The value of distinguishing the lesion for its extreme vascularity is, however, confirmed by the second case.

CASE 11.—*Aneurysmal bone cyst of clavicle:* C.M., aged 15, schoolgirl, slipped while running but regained balance, then felt a small lump over the left clavicle.

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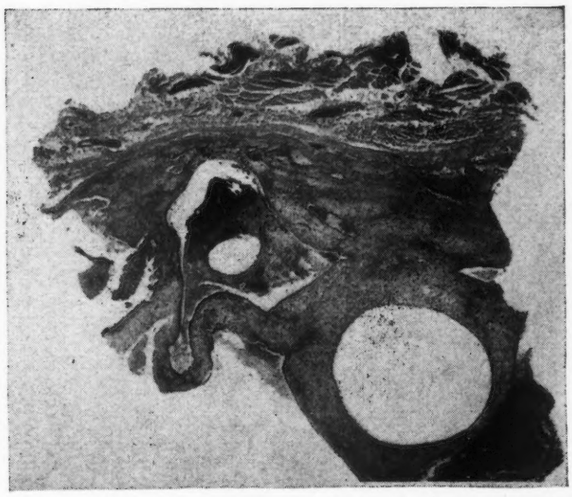

Fig. 7.—Aneurysmal bone cyst. Note the large vascular channels separated by a fibro-plastic tissue (Case 1). × 6.

Radiological examination revealed a fine honeycomb expansion and rarefaction of the inner third of the clavicle (Fig. 9). The lump increased in size rapidly over the next four months to produce a swelling 3 inches x 4 inches at the root of the neck. The swelling was generally firm but had fluctuant areas, and radiological examination revealed complete absence of the medial half of the clavicle and its replacement by a uniform dense mass with no evidence of bone formation or calcification except a thin incomplete line on the inferior aspect. The end of the remaining portion of the clavicle was ragged and slightly expanded. No other radiological abnormality was detected in the skeleton and there was no other personal or family history of bone disease. At operation the lesion was found to have a thin capsule but it appeared to extend down and be fixed to the vessels at the root of the neck. On incision of the capsule there was severe bleeding and only a small biopsy specimen was taken. Naturally with the rapid expansion of the lesion, the gross destruction of bone, and the apparent fixation to deep structures, the lesion was considered to be inoperable and malignant. The biopsy was reported as consistent with an aneurysmal bone cyst but in view of the smallness of the tissue and the formidable clinical picture a larger biopsy was requested. At a second operation much of the mass was excised, and a course of x-ray therapy followed. The mass has now shrunk and shows no evidence of progression.

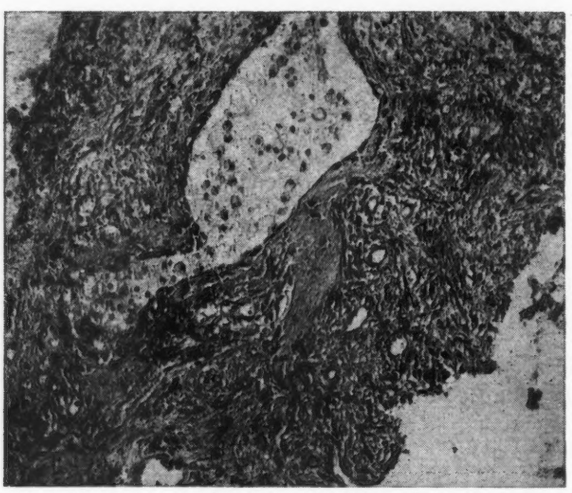

Fig. 8.—Aneurysmal bone cyst. Note the woven bone abutting on the vascular channel (Case 10). × 50.

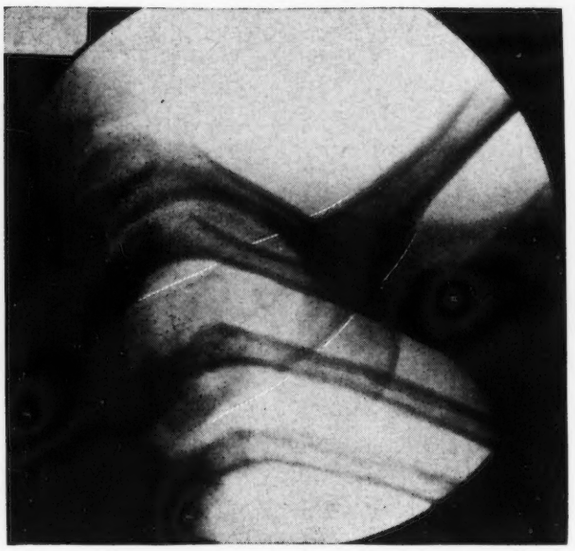

Fig. 9.—Aneurysmal bone cyst of clavicle before "blowing-up" (Case 11). Honeycomb expansion of the inner third of the clavicle, indicated by white line.

Pathological Examination

The capsule was thin but well defined and similar to the previous example. The large cavernous channels and fibrocellular trabeculæ containing spindle cells, giant cells and woven bone were also similar to those in the previous case. In addition, in the clot removed there were numerous islets of soft white tissue which showed the findings common to fibrous dysplasia—a fibrocellular tissue containing osteoclasts in places and also much new formed bone (Figs. 10 and 11).

Comment

Despite the ominous clinical picture the findings exemplify the criteria for identifying this simple condition: (1) osteoclastoma is unknown at the age of 15; (2) the rapid extension is largely accounted for by hæmorrhage from cavernous vascular channels; (3) despite the picture of gross bony destruction, the lesion has in fact evolved by expansion and still has a fibrous capsule with an inner thin line of well-formed bone, often obviously new, and still at least in part outlined radiologically by the pencil line of radio-opacity on the inferior aspect; (4) there is no histological evidence of rapid growth or cellular atypism and though large vascular channels predominate there is a mixture of osteogenic tissues in the lesion; (5) the bulk of the lesion is accounted for by clot from hæmorrhage. While the original authors show that the lesion can be treated successfully by conservative surgery, it may exceptionally be so gross as to necessitate amputation of the bone, and Lichtenstein illustrates this in a similar lesion also of the clavicle. Dr. Lichtenstein has examined the material and confirmed the diagnosis.

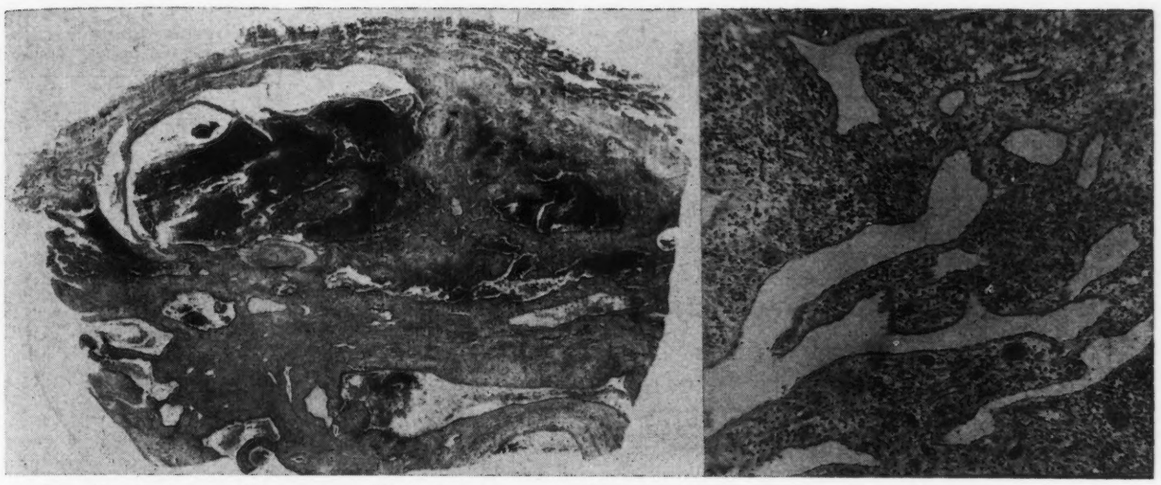

Fig. 10.—Aneurysmal bone cyst. Note the cavernous channels and fibro-plastic tissue (Case 11). × 6. Fig. 11.—Aneurysmal bone cyst. Note the vascular channels and giant cells in the cellular trabeculæ (Case 11). × 32.

For completeness we need only add to the above the additional features which the authors emphasize. No doubt in the past, even more so than fibrous dysplasia, the lesion has been confused with osteoclastoma. Unlike osteoclastoma it is a disease of childhood, adolescence or young adulthood. While, like osteoclastoma, it may occur in long bones, it is also frequent in bones where osteoclastoma is rarely or never encountered—the vertebræ, clavicle and scapula. Jaffe[8] illustrates well the characters by which it can be frequently diagnosed radiologically when encountered in a long bone—the ballooned-out distension of the periosteum at the end of a long bone.

NON-OSTEOGENIC FIBROMA

There is no difficulty in histological diagnosis of non-osteogenic fibroma and such tumours have no doubt long been recognized by most pathologists. Jaffe and Lichtenstein, however, have made an important contribution in stressing the distinctiveness and regularity of the clinical and radiological features, which my cases confirm. In the period of the survey five cases were encountered. They were encountered in the young—in four males aged 5, 13, 15 and 21, and one girl of 16. Radiologically, all have been cysts with a densely sclerosed outline scalloped or broken by well-defined, dense trabeculæ. All ran axially in the shaft coming near to one end of the bone (Fig. 12). All have been associated with few symptoms and came to light after injury, save in the girl in whom the finding was incidental in an amputation specimen of osteogenic sarcoma; all were associated with little or no expansion and were in long bones—tibia, fibula, humerus (2), femur.

Histologically they all conformed to the description of Jaffe and Lichtenstein. The tumour found accidentally consisted of interlacing bundles of well-formed fibrocellular collagen; in the remainder there was much xanthomatous change, no doubt representing a nutritional change, and in two there were occasional giant cells, especially near blood vessels.

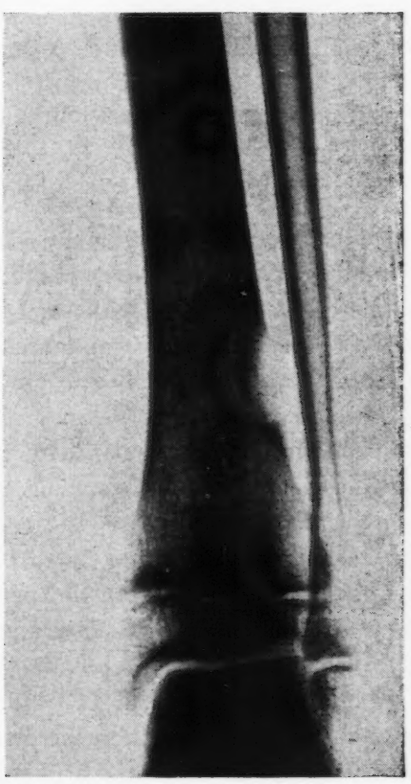

Fig. 12.—Non-osteogenic fibroma of tibia. Note the heavy scalloping round the lesion.

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Differing from the description of Jaffe and Lichtenstein, in the substance of two there were very occasional minute islets of woven bone unassociated with hæmorrhage. The adjective non-osteogenic would seem more correctly to imply a bias towards, rather than a completeness of, non-osteogenic function. Appearances of the xanthomatous tissue, the giant cells in fibrous tissue, and small spicules of woven bone were similar to those encountered in the osteoclastoma variant. Thus both osteoclastoma and non-osteogenic fibroma are regarded as osteogenic in origin. On the one hand, the osteoclastoma has an almost complete bias to osteoclasis; on the other hand, the "non-osteogenic" fibroma has an almost complete bias to fibrous formation. While both are distinctive clinico-pathological entities, one may rarely encounter tumours transitional between the two as previously described.

BENIGN CHONDROBLASTOMA

An example of this tumour, originally described by Codman, has not been encountered. Jaffe and Lichtenstein have defined its characters. The tumour originates within the epiphyseal end of a long bone (the femur, tibia and humerus are favoured in this order), is encountered in the second decade, predominantly in males, and is benign. The radiological and histological features, like the age of onset, appear to be quite distinctive from those of osteoclastoma.

ANGIOMA OF BONE

Angiomas of bone are rare tumours. Even in a large radiological practice they are likely to be encountered only in the skull or vertebræ where they often cause no symptoms. In the long bones they are occasionally encountered as sub-periosteal honeycomb lesions, more densely scalloped than the osteoclastoma, involving the shaft as well as the end and showing a much wider age distribution than the osteoclastoma. For those reasons they are unlikely to be mistaken for osteoclastomas. During the period of the survey one example was encountered in which age, site and radiological findings were similar to those in osteoclastoma. While this rarity is a collector's piece, it again serves to illustrate that osteoclastoma is not a radiological entity.

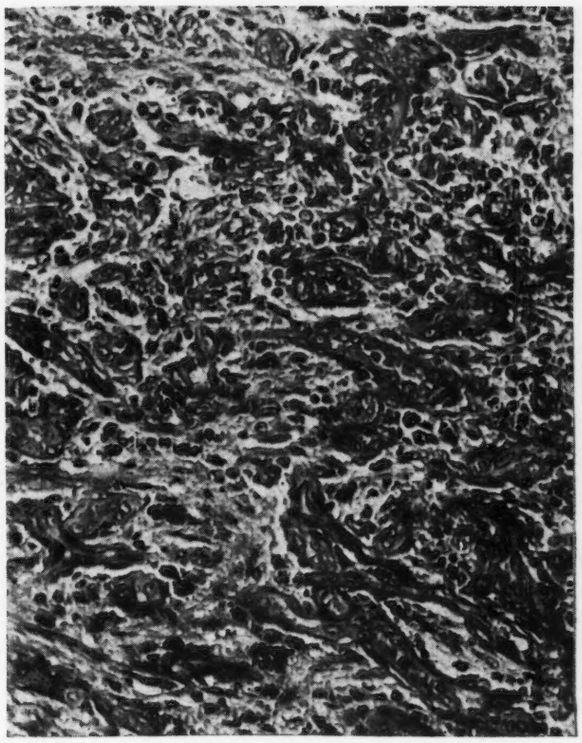
CASE 12.—*Capillary angioma of femur.* Miss N.H., aged 22, gave a history of pain and swelling of left knee for one year. Radiological examination revealed a honeycomb lesion of the lower end of the left femur (Fig. 13), which was treated by curettage and incorporation of bone chips with rapid resolution.

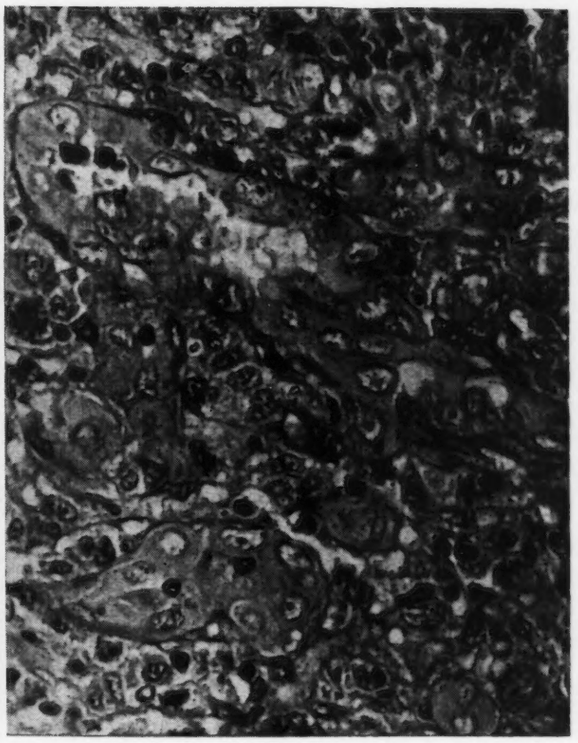
Fig. 13.—Honeycomb lesion of femur which radiologically suggested osteoclastoma but proved to be a simple angioma (Case 12).

Pathological Examination

The material was firm and white with interspersed brownish areas and areas of recent hæmorrhage. The white firmish areas consisted of relatively bloodless, compact masses of capillary channels lined by plump endothelial cells usually filling the lumen. There were also more loosely arranged areas where more of the capillaries had lumina. The capillaries were separated by a loose connective tissue showing either recent hæmorrhage or much hæmosiderin of old hæmorrhage, producing the brown colour. Well-defined fibrous and bony trabeculæ were present (Figs. 14 and 15). The large fibroplastic septa containing a variety of osteogenic tissues as seen in aneurysmal bone cysts were not present.

Thus the condition differed from aneurysmal bone cyst in that: (1) the blood channels were small and compact and mainly collapsed; (2) diverse osteogenic tissues were not present; and (3) the characteristic clamant symptomatology of "blowing up" as in Case 10 was not present. Whether aneurysmal bone cyst and cavernous angioma are separate conditions is another question.





Figs. 14 and 15.—Capillary angioma of femur. Note the capillary channels and interstitial hæmorrhage (Fig. 14, × 220). Note that many capillary channels are closed (Fig. 15, × 450).

CONCLUSIONS

Osteoclastomas and lesions associated with their differential diagnosis encountered in a five-year period in Nova Scotia have been assessed against the contributions of Jaffe and Lichtenstein; the series, though small, confirms the contributions made by Jaffe and Lichtenstein except for some views as to histogenesis. From this it is considered justified to proceed to the following general conclusions.

1. *Histogenesis of osteoclastoma.* In principle we can follow Willis's view that osteoclastoma is an osteogenic tumour with an almost complete bias to osteoclasis. Within this definition it is possible to pass in morphological declension from: (1) undoubted osteogenic sarcomas which are debatable malignant osteoclastomas, to (2) highly malignant osteoclastomas which are histologically atypical and metastasize early, to (3) classical osteoclastomas consisting largely of spindle cells and giant cells but including some fibrocellular areas and, at least on prolonged search, revealing some woven bone formation, to (4) osteoclastoma variants in which the formation of fibrous and osteoformative structures is dominant. From this latter group by virtue of age incidence, site of predilection, characteristic morphology and benign behaviour we must follow Jaffe and Lichtenstein and clearly define separate clinico-pathological entities, namely chondromyxoid fibroma of bone, benign chondroblastoma and non-osteogenic fibroma. It must also be recognized that some variants show divergent differentiation and cannot be classified under those new entities; they are rare and have a benign prognosis.

2. *Classical osteoclastoma.* This is a rare tumour having an incidence in Nova Scotia and the Canadian Prairies of the order of one per million per annum. We agree with Jaffe and Lichenstein that it is almost confined to the ends of long bones and is rare under the age of 20 and possibly unknown in childhood and adolescence. While some tumours may resolve after irradiation, this is a chance result probably due to interference with the blood supply. As a class these tumours are resistant to irradiation, and indeed irradiation is likely to stimulate the tumour and may induce frank sarcoma. The tumours show histological variation but atypism is not a precise guide to behaviour. We can agree with Jaffe and Lichtenstein that perhaps only half will yield to a single curettage and that at least one in six eventually requires amputation. The outlook is even more gloomy when irradiation is employed. They are formidable neoplasms

and their handling requires nice judgment on the part of the surgeon.

3. *Non-osteogenic fibroma* is a characteristic, simple tumour of the shaft of long bones. The adjective non-osteogenic indicates a strong bias towards, rather than a completeness of, non-osteogenic function.

4. *The aneurysmal bone cyst* is par excellence a honeycomb lesion of bone. It is not a tumour but is liable to be mistaken for one. It is no rarer than classical osteoclastoma and its resolution under irradiation has probably given rise to confidence in this treatment for osteoclastomas, while its ominous behaviour may in the past have led to unnecessary radical surgery.

5. We can agree with Jaffe and Lichtenstein that (1) except for the lower end of the femur, upper end of the tibia, and distal end of the radius, honeycomb lesions of bone are most unlikely to be osteoclastomas; (2) honeycomb lesions of bone in childhood and adolescence are probably never osteoclastomas.

6. Simple angiomas of bone may occasionally simulate osteoclastoma as to age, site and radiological findings.

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RÉSUMÉ

L'auteur s'est inspiré des travaux de Jaffe et Lichtenstein sur les ostéoclastomes pour revoir les cas qu'il a traités en Nouvelle-Ecosse de septembre 1950 à août 1955. Les tumeurs à myéloplaxes se voient rarement avant l'âge de 20 ans, et, sauf pour la mâchoire, on les trouve surtout à l'extrémité des os longs, presque toujours à l'extrémité inférieure du fémur, à l'extrémité supérieure du tibia, à la partie distale du radius et quelquefois à l'extrémité supérieure de l'humérus. L'auteur se range du côté de ceux qui prétendent que ces tumeurs proviennent de cellules formatives de tissu osseux montrant une forte tendance à l'ostéoclasie. Il est d'avis qu'une transition existe entre les tumeurs à cellules géantes et les autres tumeurs ostéogéniques. Deux cas sont rapportés illustrant la transition entre le sarcome ostéogénique et l'ostéoclastome.* Deux autres cas d'ostéoclastome classique forment l'ensemble des nouveaux cas découverts pendant la période citée plus haut. Parmi les cas antérieurs suivis au dispensaire se trouve celui d'une tumeur à myéloplaxes classique qui avait résisté à la radiothérapie et dont le traitement conservateur était venu à bout. Un autre cas d'ostéoclastome avait subi une transformation sarcomateuse sous l'influence des rayons X. Enfin, un septième et dernier cas de tumeur qui, sous l'influence de la radiothérapie, aurait manifesté une progression rapide et aurait nécessité une désarticulation. D'après Lichtenstein, la moitié de ces tumeurs se rendent à un traitement conservateur. Un tiers d'entre elles exigent l'amputation, alors que les autres indubitablement malignes ont tendance à former des métastases aux poumons. Parmi les problèmes associés figurent le fibrome chondromyxoïde, l'anévrisme kystique des os, les fibromes non ostéogéniques, les chondroblastomes bénins et les angiomes des os. Certaines de ces tumeurs peuvent présenter une image aréolaire en nid d'abeille qui peut prêter à confusion. Cependant, la distribution des lésions contribue à caractériser les tumeurs à cellules géantes. M.R.D.

*Note du traducteur: Cette transformation maligne spontanée n'est pas admise par les auteurs français.

THE EFFECT OF INTRAVENOUS HEXAMETHONIUM CHLORIDE ON BLOOD PRESSURE AND RENAL FUNCTION*

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THE EFFECTS on renal function in hypertensive patients of acute lowering of blood pressure by intravenously administered veratrum viride alkaloid (Veriloid) has been previously reported from this laboratory.[1] Acute lowering of blood pressure in the present study was produced by the intravenous administration of hexamethonium chloride. Renal clearances and electrolyte excretions were measured during an eight-hour period of acute reduction in blood pressure and in an immediately subsequent 16-hour recovery period during which the blood pressure rose toward previous control values.

Hexamethonium chloride blocks the transmission in autonomic ganglia. This pharmacological property is related to the polymethylene chain of the compound.[2] It was demonstrated by Restall and Smirk[3] that the autonomic blockade produced by hexamethonium iodide reduced

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TABLE I.

CLINICAL DATA IN PATIENTS

Patient and age	*Highest B.P. recorded*	*Duration of hypertension*	*Symptoms*	*Cardio-megaly*	*Eye grounds*	*E.C.G.*	*Protein-uria*	*Blood urea nitrogen mg./100 ml.*	*Organ decompensation*
1 51	214/142	9 years	0	+	Arteriolar spasm, A-V com-pression	Left ventricular hypertrophy	+	25	Myocardial infarct (old); cerebral vas-cular accident (sympathectomy).
2 57	250/144	3 years	Dizziness, substernal pain on exertion	+	Arteriolar spasm, A-V com-pression	Left ventricular hypertrophy	++++	44	0
3 42	248/148	10 years	Dizziness, headache, fatigue	0	Arteriolar spasm, A-V com-pression	Left ventricular hypertrophy	+	39	Myocardial infarct (old).
4 53	230/120	13 years	Headache	0	Arteriolar spasm	Left ventricular hypertrophy	0	25	0
5 42	204/132	13 years	Dyspnœa on exertion, dizziness	0	Arteriolar spasm, A-V compression	Normal	0	23	0
6 40	228/114	4 years	Precordial pain on exertion	0	Arteriolar spasm	Left ventricular hypertrophy	+	30	Congestive failure (previous).
7 55	248/128	10 years	Dyspnœa on exertion	0	Arteriolar spasm	Left axis deviation	+++	40	0
8 39	180/110	15 years	Headache	0	Arteriolar spasm, A-V compression	Left axis deviation	0	21	0
9 49	235/140	10 years	Headache, dizziness	0	Arteriolar spasm, A-V com-pression	Left ventricular hypertrophy	0	33	Subarachnoid hæmorrhage (previous).
10 56	250/120	+2 years	Weakness, dysphagia, dysphonia	+	Arteriolar spasm, A-V com-pression	Left ventricular hypertrophy	+	39	Brain stem vascu-lar lesion (old).

sympathetic arteriolar tone and peripheral resistance, and so lowered blood pressure. A review of the literature[4-9] reveals that intravenous administration of hexamethonium produces a marked reduction in blood pressure and an associated initial marked decrease in glomerular filtration rate (GFR) and renal plasma flow (RPF). The GFR and RPF return to or approach control values in one to two hours although the blood pressure continues reduced. Despite the return of GFR to control values, marked oliguria and decreased urinary sodium excretion persist up to one hour after blood pressure returns to control values. Decreased GFR is not associated with reduction of Tm PAH (p-aminohippurate). There may be slight reduction of urinary potassium excretion.

Other hæmodynamic effects of the intravenous administration[5, 6, 8, 10] of hexamethonium chloride include decreased output in the healthy heart and increased output in the decompensated heart. The reduction of peripheral resistance in cardiac decompensation is greater than in the normal. Right heart pressures are reduced in both instances.

Ford *et al.*[11] have studied the effects of long-term administration of hexamethonium. Renal function studies were performed on a group of patients in whom the mean blood pressure had been reduced 40 mm. Hg or more by orally

TABLE IIA.

RESPONSE OF THE BLOOD PRESSURE AND RENAL FUNCTION TO INTRAVENOUS HEXAMETHONIUM CHLORIDE

Patient	Dose hexamethonium in mg.	Systolic blood pressure in mm. Hg 1	2	3*	Diastolic blood pressure in mm. Hg 1	2	3	Pulse 1	2	3	GFR in ml./min. 1	2	3	Urine flow in ml./min. 1	2	3
1	50	184	130	−54	126	94	−32	72	77	+5	86	77	−9	1.82	0.31	−1.51
2	74	216	142	−74	137	103	−34	72	79	+7	70	49	−21	1.56	0.46	−1.10
3	71	207	165	−42	140	120	−20	82	92	+10	99	68	−31	1.75	0.83	−0.92
4	163	179	141	−38	113	99	−14	58	77	+19	102	71	−31	0.98	0.75	−0.23
5	75	157	129	−28	104	89	−15	79	88	+9	179	135	−44	1.51	0.89	−0.62
6	73	167	138	−29	97	90	−7	75	87	+12	157	142	−15	2.80	1.03	−1.77
7	11	170	128	−42	103	92	−11	90	88	−2	82	84	+2	0.87	0.59	−0.28
8	39	160	135	−25	113	102	−11	90	95	+5	127	126	−1	0.76	0.61	−0.15
9	61	196	144	−52	130	110	−20	74	77	+3	96	85	−11	1.28	0.77	−0.51
10	74	217	149	−68	113	89	−24	68	67	−1	83	70	−13	1.96	0.49	−1.47
Mean difference ± S.E.M.			−45 ± 5			−19 ± 3			+7 ± 2			−17 ± 5			−0.86 ± .19	
P value			<.001			<.001			<.01			<.01			<.01	

*Column 1—Control period (9 a.m. to 5 p.m.) values averaged.
Column 2—Experimental period (9 a.m. to 5 p.m.) values averaged.
Column 3—Difference (2 - 1).

administered hexamethonium for from seven days to one month. In the supine position there was a reduction of blood pressure, rate of urine flow and sodium and potassium excretion, without change in GFR, RPF or Tm PAH. With ambulation, there was a further reduction in blood pressure, urine flow and electrolyte excretion; a pronounced fall in GFR, RPF and Tm PAH was produced.

The intravenous administration of hexamethonium chloride produces a pronounced fall in blood pressure and an associated decrease of GFR, which subsequently returns to control values although blood pressure remains reduced. There is a renal retention of sodium and water. In general, the results of our study confirm these conclusions.

MATERIALS AND METHODS

Ten white male patients with benign essential hypertension were studied. Clinical data including age, duration of hypertension, symptomatology, cardiac enlargement, electrocardiographic changes, changes in the optic fundi, blood urea nitrogen, proteinuria and organ decompensation are given in Table I. The cerebral vascular accident in patient 1, the congestive failure in patient 6, the subarachnoid hæmorrhage in patient 9 and the brain stem vascular lesion in patient 10 had all occurred six to 18 months before our study. The sympathectomy on patient 1 had been performed five years previously.

In each patient the renal responses to the intravenous administration of hexamethonium chloride were studied during a 12-day period, throughout which the patient was maintained on a constant intake of sodium and potassium to obviate any dietary influence on urinary electrolyte output. To ensure uniform intake, each of the items of the diet was purchased in one lot and identical weighed servings were given for each breakfast, dinner and supper.

There were five test days during the 12-day study. On the test day, the patient was kept in bed and urine was collected by in-lying catheter over two-hour intervals for eight hours, 9 a.m. to 5 p.m. For the remainder of the 24 hours of observation, 5 p.m. to 9 a.m., the urine was collected as one 16-hour specimen. Blood pressure was measured at 9 and 11 a.m., and at 1, 3 and 5 p.m.; and blood specimens were taken at 10 a.m., 12 noon, and at 2 and 4 p.m. A preliminary control test without laboratory determinations on Day 3 accustomed the patients to the procedure. Day 5 and Day 10 were control days. On Day 7 and Day 12, intravenous hexamethonium chloride was given during the eight-hour period 9 a.m. to 5 p.m. During the administration, the blood pressure and pulse were determined every four minutes.

Urine volumes were measured and aliquots analyzed for sodium, potassium and creatinine for each of the two-hour periods. Similar determinations were made on the blood specimens. The GFR for each period was calculated from

TABLE IIB.

RESPONSE OF BLOOD PRESSURE AND RENAL FUNCTION TO INTRAVENOUS HEXAMETHONIUM CHLORIDE

Patient	*Urinary Na. excretion μ mEq./min.* 1	2	3*	*Na. intake g./24 hr.* 1	2	3	*Urinary K. excretion μ mEq./min.* 1	2	3	*K. intake g./24 hr.* 1	2	3	*Serum Na. mEq./l.* 1	2	3	*Serum K. mEq./l.* 1	2	3
1	140	17	−123	1.93	1.99	.06	60	37	−23	2.65	2.73	.08	142	140	−2	4.3	3.6	−0.7
2	63	5	−58	2.18	2.35	.17	48	36	−12	2.93	3.08	.15	142	143	+1	4.3	4.5	+0.2
3	52	3	−49	1.45	1.48	.03	76	64	−12	3.21	3.07	.14	139	139	0	4.7	4.7	0
4	54	51	−3	1.91	1.01	.90	30	58	+28	2.82	1.92	.90	142	141	−1	3.9	4.3	+0.4
5	98	51	−47	2.53	2.51	.02	56	65	+9	3.20	3.17	.03	139	136	−3	4.3	4.3	0
6	115	24	−91	2.10	2.34	.24	81	87	+6	4.38	3.21	1.17	140	140	0	4.1	4.1	0
7	30	12	−18	0.92	0.87	.05	53	45	−8	2.64	2.68	.04	139	136	−3	4.5	4.5	0
8	134	62	−72	1.63	1.45	.18	59	72	+13	2.15	2.27	.12	139	138	−1	4.7	4.9	+0.2
9	151	46	−105	2.07	2.24	.17	80	83	+3	2.78	2.97	.19	137	137	0	4.4	4.7	+0.3
10	119	17	−102	1.55	1.44	.11	70	57	−13	3.15	2.91	.24	139	140	+1	4.7	4.8	+0.1
Mean difference ± S.E.M.			−67 ± 12			0.19 ± .08			−1 ± 5			0.31 ± .12			−1 ± .5			+0.1 ± .1
P value			< .01			< .05 > .02			> .10			< .05 > .02			> .05			> .10

*Column 1—Control period (9 a.m. to 5 p.m.) values averaged.
Column 2—Experimental period (9 a.m. to 5 p.m.) values averaged.
Column 3—Difference (2 - 1).

the urine flow and the urine and serum creatinine levels by the method of Schoch and Camara.[12] Urine and serum creatinine levels were determined by the method of Folin as modified by Hawk, Oser and Summerson.[13] The sodium and potassium intakes on control and experimental days were determined on homogenized aliquots of all the meals to provide total 24-hour values (9 a.m. to 9 a.m.). All electrolyte determinations were performed on the Perkin-Elmer flame photometer, Model 52 C, employing the lithium internal standard method of analysis.

Hexamethonium chloride solution was diluted in 5% aqueous glucose (1.25 mg. per ml.). Slow intravenous administration by syringe was begun at 9 a.m. on the experimental days and was continued until a pronounced fall in blood pressure occurred. If the blood pressure rose during the 9 a.m. to 5 p.m. period, more hexamethonium was administered. The average of the two total doses for each patient is shown in Table IIa.

RESULTS

Tables IIa and IIb present the results of the eight-hour (9 a.m. to 5 p.m.) control and experimental periods of study. Table III presents the results of the 16-hour (5 p.m. to 9 a.m.) control and experimental periods. In each table the average of all determinations for both control days appears in column 1 and for both hexamethonium days in column 2. Rates of urine flow and GFR are given in millilitres per minute (ml./min.). Electrolyte outputs are presented in terms of micro-milliequivalents per minute (μmEq./min.). Electrolyte intakes are given in terms of grams per 24 hours (g./24 hr.). The results have been analyzed statistically and the mean differences with standard error of the mean between the control and experimental periods are presented.

Hexamethonium produced a marked and significant lowering of both the systolic and diastolic blood pressure (Tables IIa and IIb). The heart rate was increased. There was a significant reduction in the GFR in all patients with the exception of Cases 7 and 8 in which there was relatively little change. A marked reduction in the rate of urine flow occurred in all patients. Only Case 4 failed to have a profound decrease in the rate of sodium excretion. The changes in the rate of potassium excretion and in the serum electrolytes were not significant. There was no significant difference between the electrolyte intakes on control and experimental days. The urinary output of electrolytes could not, therefore, be influenced by change of intake.

In Table III it is seen that in the 16 hours after termination of hexamethonium administration the systolic blood pressure was still significantly reduced in five cases and the diastolic in seven cases. The GFR and urinary sodium excretion however, although still reduced, were returning

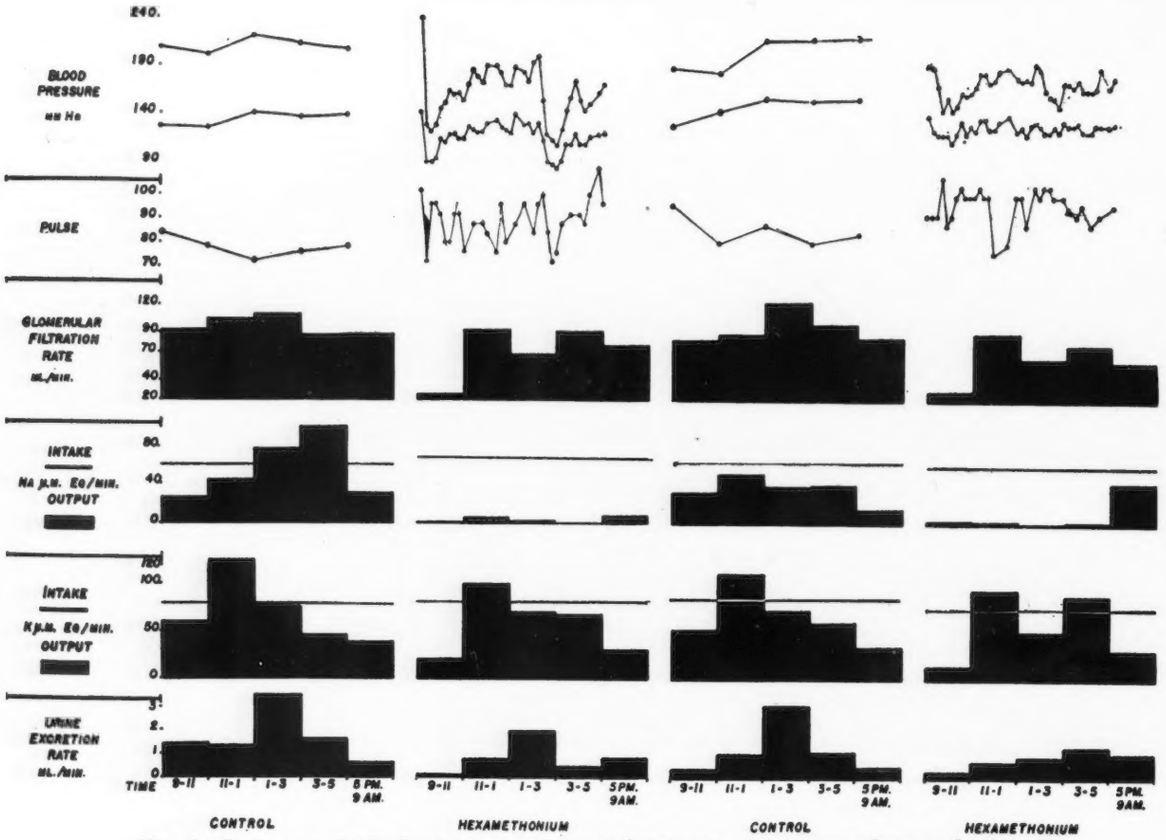

Fig. 1.—Response of blood pressure and renal function to intravenous hexamethonium in patient 3. Data presented for two-hour periods (9 a.m. to 5 p.m.) and 16-hour periods (5 p.m. to 9 a.m.). Note the marked initial reduction in GFR and potassium excretion which rise to control levels during the second two-hour period on the experimental days. The marked reduction in urine flow and sodium excretion persists throughout the experimental periods.

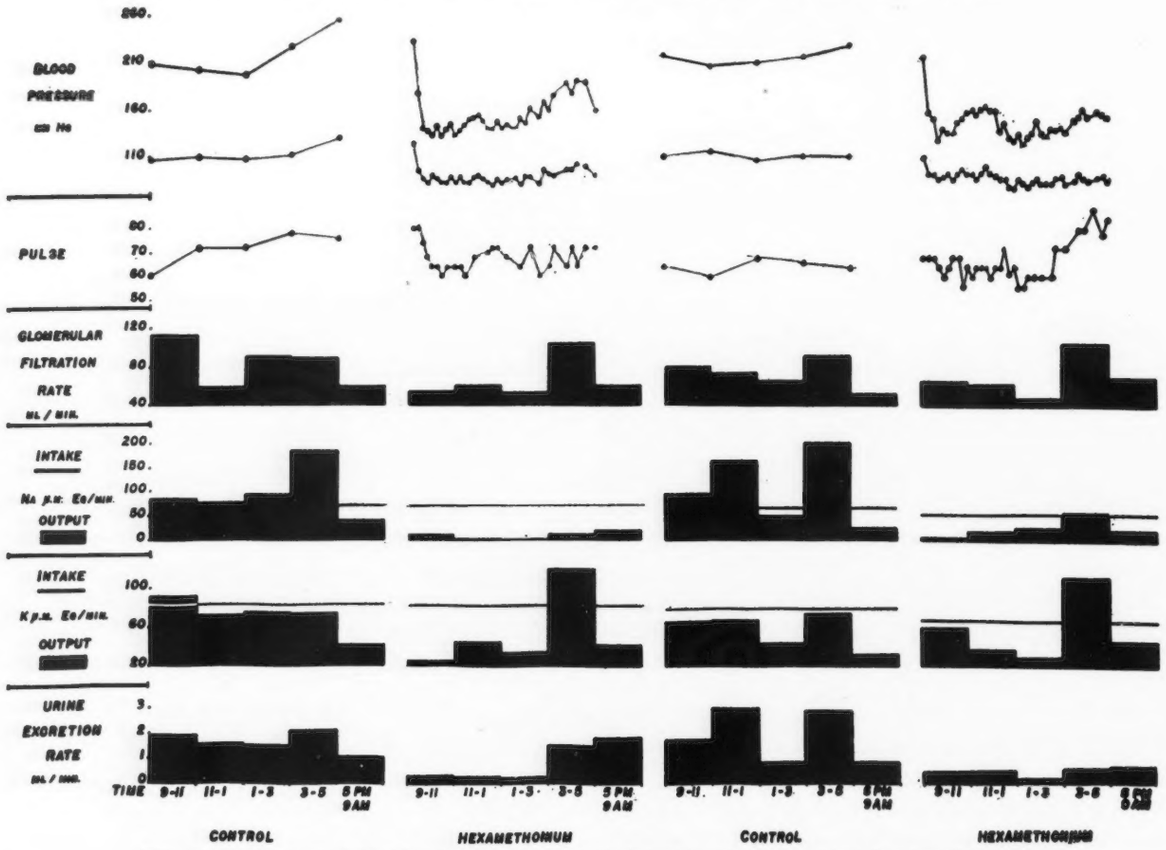

Fig. 2.—Response of blood pressure and renal function to intravenous hexamethonium in patient 10. Data presentation similar to Fig. 1. Initial reduction in GFR and persistent reduced sodium excretion and urine flow are to be observed.

TABLE III.

BLOOD PRESSURE AND RENAL FUNCTION FOLLOWING HEXAMETHONIUM CHLORIDE

Patient	*Systolic† blood pressure in mm.Hg* 1	2	3*	*Diastolic† blood pressure in mm.Hg* 1	2	3	*Pulse†* 1	2	3	*GFR in ml./min.* 1	2	3	*Urine flow in ml./min.* 1	2	3	*Urinary Na. excretion μ mEq./min.* 1	2	3	*Urinary K. excretion μ mEq./min.* 1	2	3
1	183	180	−3	124	124	0	83	64	−19	61	52	−9	0.74	0.50	−0.24	32	8	−24	28	13	−15
2	208	193	−15	142	131	−11	72	76	+4	57	42	−15	1.27	0.93	−0.34	68	10	−58	37	24	−13
3	201	174	−27	127	115	−12	88	84	−4	87	71	−16	0.55	0.97	+0.42	24	26	+2	36	31	−5
4	166	158	−8	118	98	−20	64	68	+4	93	71	−22	0.69	0.33	−0.36	38	10	−28	24	32	+8
5	152	132	−20	96	92	−4	79	102	+23	127	92	−35	0.70	0.86	+0.16	38	46	+8	28	23	−5
6	162	137	−25	119	95	−24	102	91	−11	116	108	−8	0.71	0.84	+0.13	20	15	−5	36	38	+2
7	152	148	−4	94	100	+6	86	100	+14	64	77	+13	0.65	0.76	+0.11	20	21	+1	29	32	+3
8	160	122	−38	108	94	−14	100	98	−2	113	120	+7	0.40	0.40	0	27	29	+2	21	29	+8
9	170	164	−6	120	110	−10	74	87	+13	79	74	−5	0.52	0.59	+0.07	31	32	+1	30	36	+6
10	199	208	+9	113	103	−10	72	76	+4	57	66	+9	1.00	1.24	+0.24	32	21	−11	36	44	+8
Mean difference ± S.E.M.	−14 ± 4			−10 ± 3			+3 ± 4			−8 ± 5			+0.02 ± .08			−11 ± 6			0 ± 3		
P value	< .02			< .01			> .10			> .10			> .10			> .10			> .10		

*Column 1—Control period (5 p.m. to 9 a.m.) values averaged.
Column 2—Experimental period (5 p.m. to 9 a.m.) values averaged.
Column 3—Difference (2 - 1).
†Blood pressure and pulse taken 9 a.m., end of 16-hour period.

to control values. The rate of potassium excretion showed no significant change from control values.

Figs. 1 and 2 show the complete results of the 24-hour studies in Cases 3 and 10 respectively. Electrolyte intakes in these figures are expressed in micro-milliequivalents per minute (μ.mEq./min.) for greater convenience. The well-marked initial reduction of blood pressure can be observed in both figures. This was not maintained in Case 3 (Fig. 1), and a second injection of hexamethonium was required which caused a second precipitous fall in blood pressure. The GFR in both cases showed a marked initial reduction, but both returned to control values although the blood pressure remained reduced. This occurred more rapidly in Case 3. The marked reduction in the urinary sodium excretion and urine flow, and the failure to return to control levels within the eight-hour experimental periods, can be seen in both figures.

DISCUSSION

The intravenous administration of hexamethonium chloride to hypertensive patients produces autonomic ganglionic nerve block, loss of arteriolar sympathetic tone, arteriolar dilation and rapid fall of blood pressure. The renal vessels do not initially participate in this dilation, for it is reported that the renal vascular resistance is not reduced.[6] The RPF consequently falls, which in turn reduces the GFR. This would indicate some degree of autonomy in the control of renal arteriolar tone; with a sudden fall of blood pressure, reflex mechanisms may maintain renal vascular tone. After some time, however, the renal vascular resistance also decreases, which restores the renal portion of the total blood flow toward normal. This restores the GFR.

The rate at which this decrease of renal vascular resistance and return of GFR to control levels occurs appears to be variable. Cases 7 and 8 showed no significant reduction of GFR during the eight-hour period of reduced blood pressure. These patients apparently had a rapid loss of reflex renal arteriolar tone. In all other cases, however, the GFR remained significantly reduced throughout the period of reduced blood pressure, indicating a persistence of renal vascular resistance greater than the general vascular resistance. The GFR returned toward control values more rapidly in Case 3 than in Case 8 (Figs. 1 and 2). We have previously shown that reduction of blood pressure with veratrum viride alkaloid produced little or no change in GFR during the eight-hour experimental period[1] although the reduction in diastolic blood pressure was quantitatively similar to that produced in the present study. Reduction of systolic pressure was slightly less. Reduction in renal vas-

cular resistance may occur more rapidly and to a greater degree when acute blood pressure reduction is accomplished with the veratrum alkaloid.

When the blood pressure returned toward control levels in the 16-hour recovery period, reduction in GFR persisted for a longer period than in the veratrum studies.

The other pertinent effects produced by this acute lowering of blood pressure are the marked reduction in urine flow and sodium excretion. Urine flow exceeded or approached control levels during the 16-hour recovery period except in Case 4. In this patient the diastolic pressure continued low. The same patient failed to show a reduction of sodium excretion until the 16-hour recovery period. All other patients showed a marked reduction of urinary sodium which returned to or approached control values in the recovery period with the exception of Case 2. In this patient, the low sodium excretion persisted for the full 24 hours. Cases 4 and 2 thus appear to have atypical responses.

The mechanisms of production of the oliguria and sodium retention are obscure. It is unlikely that they are due to reduction of GFR alone, for they persist despite its return to control values. They cannot be due to secretion of antidiuretic hormone, for Murphy and Stead have shown that ADH does not produce tubular reabsorption of sodium.[14] They may be due to liberation of excess aldosterone from the adrenal cortex. There was no increase in potassium excretion. Excess aldosterone liberation would therefore seem unlikely. They are not due to a decrease in the number of functioning nephrons.[4] Moyer and Mills[7] have suggested that hexamethonium chloride does not produce as great a sympathetic ganglionic block of the renal autonomic nerves as elsewhere, for some degree of renal sympathetic vasoconstrictor tone is maintained. This tone (and increased vascular resistance) may later decrease in the glomerular vessels but persist in the tubular vessels, leading to some degree of tubular ischæmia, interference with tubular enzyme systems and subsequent increased tubular reabsorption of sodium and water. In comparison with our previous veratrum study, hexamethonium produced a greater degree of oliguria and sodium retention, and a slower return to control levels of urine flow and sodium excretion during the recovery period.

Summary and Conclusions

1. The response of renal function to the acute lowering of blood pressure by intravenous administration of hexamethonium chloride has been studied in 10 patients with essential hypertension.

2. There was a marked initial reduction of GFR which slowly returned toward control values.

3. Oliguria and sodium retention were produced.

4. The possible mechanisms of these effects are discussed.

5. The reduced GFR, oliguria and sodium retention were quantitatively greater than those previously produced with veratrum alkaloid. Moreover, the return of GFR to control values appeared to be slower after hexamethonium than after veratrum.

6. There was no significant effect on pulse, serum electrolytes or urinary potassium excretion.

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Résumé

Cet article rapporte les résultats obtenus dans le coefficient d'épuration et l'excrétion d'électrolyte pendant une période d'abaissement soudain et prolongé de la tension artérielle par l'administration de chlorure d'héxaméthonium. En plus de diminuer la tension artérielle, ce médicament pendant une heure ou deux au début de son action cause une réduction du taux de filtration glomérulaire et de la circulation rénale du plasma. L'héxaméthonium contribue à diminuer le débit cardiaque du cœur normal et à augmenter celui du cœur en défaillance. Ces études ont été faites sur 10 malades du sexe masculin souffrant d'hypertension essentielle bénigne. L'héxaméthonium fut administré lentement par voie intraveineuse en solution de 5%. Bien que ce composé abolisse le tonus sympathique des artérioles et amène une chute de tension par leur dilatation, il semble que les vaisseaux rénaux échappent à cette action au début. Après un certain temps, ces vaisseaux cèdent eux aussi et rétablissent ainsi la circulation rénale en rapport avec celle du reste de l'organisme. Pendant cette période de décalage, le taux de filtration glomérulaire diminue, causant ainsi une diminution de la formation d'urine et de l'excrétion de sodium. Cependant, d'autres mécanismes doivent entrer en jeu puisque cette oligurie et cette rétention sodique persistent après le retour à la normale du TFG. Les auteurs suggèrent la production excessive d'aldostérone par les surrénales comme explication possible, mais peu probable. Ces perturbations sont plus marquées avec l'héxaméthonium qu'avec le veratrum viride. M.R.D.

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DIABETIC RETINOPATHY*

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THE INCREASE in life expectancy of diabetics which has occurred in the insulin era and which has been further augmented by the general advances in the understanding and treatment of metabolic disorders has led to an increase in the degenerative complications of diabetes. Such is apparently the case with diabetic retinopathy, a complication which intimately concerns the ophthalmologist. In his own private practice Friedenwald[1] in 1950 observed that the incidence of retinopathy had increased threefold as compared to 1924, while the incidence of cataracts and of glaucoma did not change significantly in the same groups of patients. On the other hand, a study by Vogelius[2] indicates that there is a marked increase in the frequency of retinopathy in proportion to the number of diabetics, which he states is more than the increased survival time for diabetics could account for. He suggests that this may in part be due to less rigid control of diabetics. However, there is a good deal of data comparing rigidly controlled diabetics with those in whom the blood sugar is allowed a greater degree of fluctuation, which fail to support the hypothesis that the degree of control of blood sugar significantly affects the incidence of retinopathy. Clinical studies by Waite and Beetham[3] have shown that retinopathy is related to the duration of the diabetes and not to the age of the patient or the severity of the disease. Very few patients who have had the disease for more than 15 years will escape without some evidence of retinopathy.

Following decades of controversy it is now well established that diabetic retinopathy presents a characteristic ophthalmoscopic picture, which was first described by Jaeger in 1855 and more extensively by Leber in 1875. The classic studies of Hirshberg in 1895 helped resolve the arguments that followed as to whether this condition was not the same as the so-called albuminuric retinopathies. Hirshberg pointed out the differences in the ophthalmoscopic pictures and also showed that the course and morphology of these diseases differed, many patients with diabetic retinopathy having neither albuminurian or hypertension. The controversy regarding the relationship between diabetic retinopathy and arteriosclerosis has apparently been resolved as well (as far as such arguments are ever capable of resolution). Waite and Beetham have shown that in approximately 50% of patients with retinopathy they could find no ophthalmoscopic evidence of retinal arteriosclerosis. Friedenwald[4] examined the eyes of patients with retinopathy microscopically and found no morphological evidence of disease of the whole retinal tree in about half of these cases.

In 1877 Nettleship,[5] in one of the first pathological reports on diabetic retinopathy, observed capillary aneurysms, but this observation received little attention until Ballantyne and Loewenstein[6] in 1944, examining flat, unstained retinas, noted many capillary aneurysms present. Employing serial sections, Friedenwald[7] confirmed this observation and later developed special staining techniques to study flat, unsectioned retinas. These studies revealed numerous minute saccular aneurysms in the retinas of many diabetic patients. The aneurysms are often thin-walled, but others show thickening and hyalinization. They are frequently surrounded by a cluster of hæmorrhages and/or exudates, which would indicate that these aneurysms develop at points of local weakness in the vessel wall or are at least associated with these points. These sites are usually at the capillary bifurcation or at the sharp bends of the capillary, and as such are similar to the congenital berry aneurysms. Where the micro-aneurysm forms on the convex surface of the bend, it is not connected by a stalk, but lies directly on the capillary. Friedenwald concluded that they must therefore arise from an outpouching of the vessel wall and not from endothelization of a hæmorrhage.[8] The aneurysms are frequently too small to be visible with the ophthalmoscope, but when seen are usually located at the posterior pole of the eye and may vary greatly in number. They may be the only ophthalmoscopic evidence of diabetic retinopathy or may be associated with the round hæmorrhages and waxy exudates characteristic of this disease. By closely following-up a case, one can observe that an aneurysm may disappear altogether or become converted into a sharply outlined white spot. These spots probably represent hyalinized aneurysms.

Although these micro-aneurysms are most frequently found in diabetes, they have occasion-

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ally been found in other disease processes. Ashton[9] and Wexler and Branower[10] have seen them in retinas of patients with malignant hypertension and even in normal eyes, but the latter is a very rare occurrence. Becker and Post[11] occluded the central retinal vein in experimental animals and were able to produce micro-aneurysms. However, most of these aneurysms were fusiform or varicose, while the characteristic features of diabetic micro-aneurysms are their saccular form and their presence in uninjured portions of the retina. Friedenwald concluded that these aneurysms represent a primary vascular lesion in the retina, while in other diseases they occur in response to local injury.

Once the micro-aneurysm of diabetic retinopathy was established as part of a specific disease entity, it followed that other organs should be examined in an effort to determine whether vascular changes of a similar nature could be observed. Although the results have been rather unrewarding, one must bear in mind that the structure of the retina makes it particularly suitable for a study of its capillary network, while techniques such as flat retinal preparations are not applicable to other organs. Friedenwald and Day,[8] using the corneal microscope, studied the conjunctival vessels in 60 cases of diabetic retinopathy and were able to find an aneurysm present in only one patient. They also examined the capillary loops of the fingernail beds in a similar group of patients and found micro-aneurysms in three cases, but they felt that they could not absolutely eliminate trauma as the basis of these lesions. Reports of studies in other organs are singularly lacking, probably because of the large number of serial sections which would be required.

Kimmelstiel and Wilson[12] were the first to report on the frequent occurrence of a renal lesion in diabetes of long duration. These lesions characteristically show hyaline nodules situated at or near the periphery of the glomerular tuft and hyaline strands between and surrounding the glomerular capillaries. Allen[13] noted enlarged and dilated capillaries in some of these glomerular lesions. It was soon observed that there was a close correlation between the Kimmelstiel-Wilson lesions and retinopathy. In a series of patients with diabetic nephropathy studied by Henderson, Sprague and Wagener,[14] 80 to 90% had diabetic retinopathy. Ashton and Day, in separate studies, confirmed these findings. Post-mortem studies have shown that approximately 50% of patients with retinopathy have some evidence of diabetic nephropathy and that the frequency of both lesions increases with age, but to a much greater extent with the duration of diabetes mellitus. Friedenwald and Ashton did histochemical studies on these renal and retinal lesions and concluded that there was a striking similarity in their staining characteristics. Both types of lesions stained with a periodic-acid Schiff reagent.[15] The assumption that there is a close relationship between intercapillary glomerulosclerosis of Kimmelstiel-Wilson and the micro-aneurysms is probably a valid one: they are both specific lesions of a vascular nature occurring in diabetes. But we cannot conclude that the retinopathy precedes or follows the nephropathy or that there is any correlation between the degree of severity of these two lesions.

There is general agreement that hypoinsulinism is not the sole metabolic disorder involved in diabetes mellitus. Price, Cori and Colowick[16] established the existence of an antagonism between the pancreas and pituitary. It has also been shown that partially pancreatectomized dogs develop diabetes to a more severe degree than do completely pancreatectomized ones.

Following the advent of ACTH and cortisone and their widespread clinical use, reports began appearing in the literature regarding the effects of these hormones in diabetic patients. As one might anticipate because of their gluconeogenic action, prolonged administration of these hormones markedly influences the diabetic state. Exacerbations of the retinal complications can also be observed. During pregnancy where there is hyperactivity of the adrenal cortex and a corresponding increase in the severity of diabetes, an exacerbation of retinopathy is often observed. Following delivery or the termination of pregnancy, a remission of this retinal condition may occur. Hoet,[17] studying the chromatographic patterns of the amniotic fluid from diabetic females, found high concentrations of 17-hydroxycorticosterone and other cortisone-like substances, while normal amniotic fluids showed no evidence of any steroid. This may be due to an excessive adrenal cortical activity in the diabetic mother as compared to the non-diabetic pregnant female, or a hyperactivity of the infant's adrenal cortex. A Cushing-like syndrome may therefore explain many of the features found in the excessively large infants born to diabetic

mothers. Infection has also been shown to aggravate retinopathy,[18, 19] and adrenalectomy has been followed by an improvement in the ophthalmoscopic picture.[20] Similarly, a postpartum pituitary necrosis[21] and testosterone administration[22] have been reported to alleviate retinopathy. Mason and Sprague[23] found a high excretion of 17-hydroxycorticosterone (Kendall's Compound F; hydrocortisone) in the urine of a patient with severe diabetes mellitus, while Dobriner and associates,[24] in analyzing the steroids in the urine of normal subjects, were unable to show the presence of this compound. They concluded that in the patient studied by Mason and Sprague this steroid was formed in large amounts by the adrenal gland.

Following the daily intramuscular administration of 7.5 mg. of cortisone to rabbits for a period of from two to three weeks, Rich, Berthrong and Bennet[25] observed renal lesions closely resembling Kimmelstiel-Wilson intercapillary glomerulosclerosis. If rabbits were previously made diabetic by alloxan administration, the yield of these lesions could be markedly increased,[26] but attempts at the experimental production of retinopathy by similar means have been unrewarding. Rich[27] has found typical Kimmelstiel-Wilson lesions in the kidneys of a non-diabetic patient who had undergone long and intensive treatment with ACTH.

These observations raised the question of the role of the adrenal cortex in the production of Kimmelstiel-Wilson lesions and retinal microaneurysms. Friedenwald[28] postulated an interaction between the diabetic metabolic abnormality and adrenal cortical function. He suggested a possible hyperadrenal function in diabetics with retinopathy as compared to those without retinopathy. Studies were carried out at the Wilmer Institute of Ophthalmology in an effort to test this hypothesis, and the results show a significantly increased urinary 17-hydroxyketosteroid excretion in diabetics with retinopathy and a decreased excretion in those without retinopathy.[29]

Reports have recently appeared in the literature which would implicate mucoid metabolism in the pathogenesis of diabetic retinopathy. The work of Jacobs,[30] Glick,[31] and Layton[32] indicates that both insulin and cortisone are involved in mucoid metabolism. McManus[33] suggested on a morphological basis that such a disturbed metabolism might be a cause of both the renal and retinal lesions of diabetes.

It would therefore appear that one of the pathways leading to the production of these lesions is a disturbance of mucoid metabolism induced by diabetes and exacerbated by adrenal hyperfunction.

The enzymatic mechanisms of mucopolysaccharide formation are currently being investigated at the Wilmer Institute of Ophthalmology.[34] We are also engaged in the study of the blood proteins and polysaccharides in alloxan diabetic animals as well as diabetic patients. A good deal of work on retinopathy remains to be done, but we can now anticipate the resolution of some of the metabolic problems associated with the disease process.

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OPPONENS TRANSFER*

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THE ABILITY to oppose the thumb is a very important acquisition of man. Following injuries to the median nerve, direct trauma to the thenar muscles, and poliomyelitis, the power of opposition may be lost. The hand assumes the simian position with the thumb lying in line with the fingers, and its prehensile activity is limited to that which can be achieved by flexion of the fingers alone. The hand can only grasp and hold large objects with difficulty; picking up small objects is almost impossible; the doing up and undoing of buttons becomes a herculean task.

Many methods of restoring opposition to the thumb have been described. Probably the best of these is Thompson's[1] modification of Royle's[2] operation—it is simple, effective and reliable. Thompson's operation has been employed in the Orthopædic Service of the Toronto General Hospital over the past five years to restore opposition of the thumb in patients suffering from the effects of poliomyelitis. The results have been very gratifying, but in order that restoration of opposition of the thumb will at the same time restore an effective pinch and grasp, several other factors have to be taken into consideration.

The purpose of this paper is to describe the technique that has been employed and the additional tendon transfers that are sometimes necessary to restore effectively the grasping mechanism of the hand.

Basically the operation consists of transposing the insertion of one of the flexor sublimis tendons to the neck of the first metacarpal. The sublimis tendon loops around the remaining flexor tendons and the distal edge of the volar carpal ligament prevents the tendon from migrating proximally. The transposed tendon, when it contracts, pulls the thumb across the palm, rotates the metacarpal, and reproduces the action of opposition (Fig. 1). Obviously the flexor sublimis chosen as the motor must be of normal or near normal power and the flexor profundis to the same finger must be of normal strength, so that the power of flexion of the fingers is not grossly interfered with by the transfer.

The flexor digitorum sublimis of the fifth finger should not be used as a motor. The power of the grip is mostly a function of the ulnar side of the hand. If the flexor digitorum sublimis of the fifth finger is used, the grip tends to be weakened. The flexor digitorum sublimis of the index finger should not be used because the act of pinching involves flexion of the proximal interphalangeal joint with extension of the terminal phalanx—the sublimis action (Fig. 2). The flexor sublimis to either the third or fourth digit may be used. The flexor sublimis to the ring finger is the most ideally suited. If both are weak, both the third and fourth may be used together. If the opponens pollicis is the only muscle paralyzed, the sublimis transfer by itself gives excellent results (Figs. 3 and 4). However, opposition of the thumb and the ability to pinch and grasp depends not only on the opponens pollicis, but also

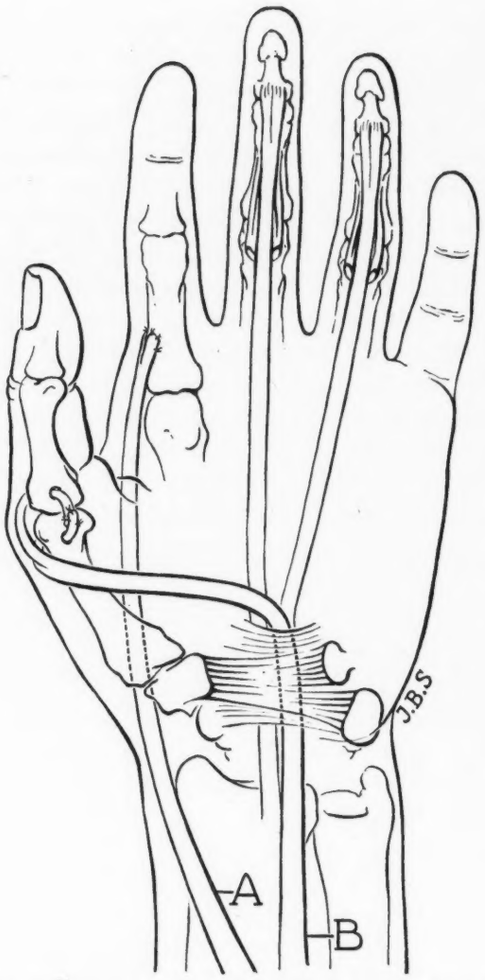

Fig. 1.—Diagrammatic representation of the tendon transfers commonly employed. The flexor digitorum sublimis (B) of the ring finger is transferred subcutaneously to the thumb, and sutured to the neck of the first metacarpal and the base of the proximal phalanx. The distal edge of the volar carpal ligament prevents the tendon from migrating proximally up the forearm. To restore the action of the first dorsal interosseous, the flexor sublimis tendon to the middle finger can be transferred subcutaneously across the radial side of the forearm and up the dorsum of the hand, and sutured to the insertion of the first dorsal interosseous (A).

*From the Orthopædic Service, Toronto General Hospital.

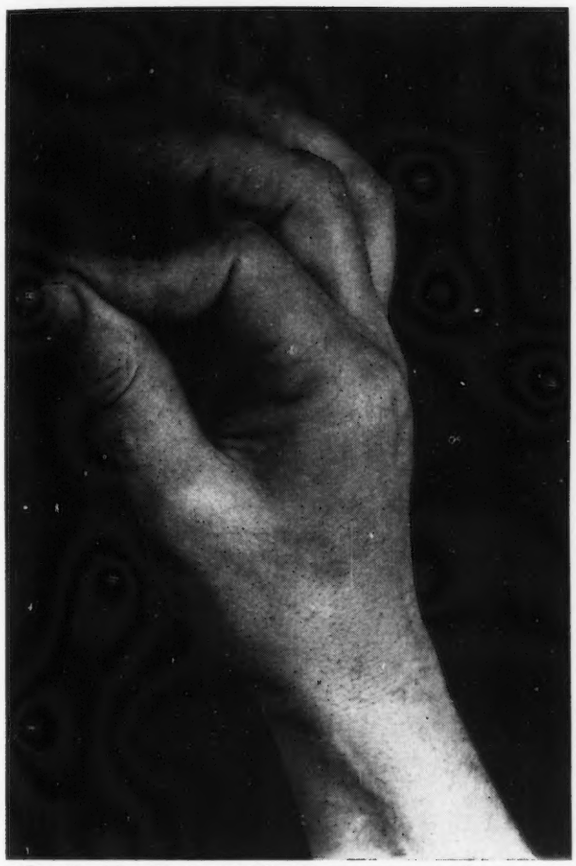

Fig. 2.—The "pulp-pinch". The common pinching action is opposition and apposition of the pulp of the thumb to the finger.

on the intricate co-ordination of several muscles, particularly the abductors of the thumb, the short flexor, the adductor pollicis and the first dorsal interosseous. In order to ensure a successful outcome of the operation, these other muscles must be assessed carefully. If they are weak or paralyzed, their action must be reinforced or replaced.

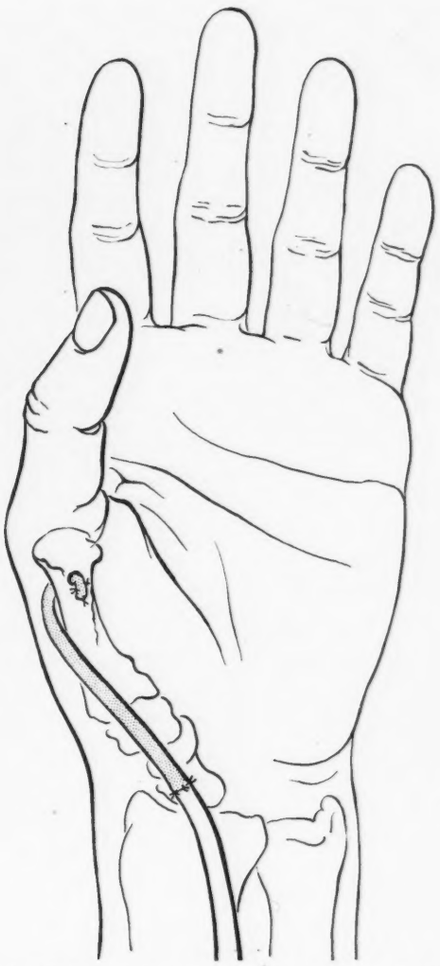

Fig. 6.—Palmaris longus may be used to replace the paralyzed abductors. It can be attached by means of a free tendon graft to the neck of the first metacarpal.

If the abductors of the thumb are paralyzed, no true opposition is possible. If the tendon transfer is performed in the presence of paralyzed abductors, the thumb can only be pulled across the

Figs. 3 and 4.—Thompson's opponens transfer performed for isolated paralysis of the opponens. In Fig. 3 the thumb is held by the side of the hand; Fig. 4 shows the degree of rotation and opposition of the thumb made possible by this operation. Fig. 5.—When the abductors of the thumb are paralyzed, no true opposition is possible. The thumb is pulled across the hand with the side of the thumb touching the palm.

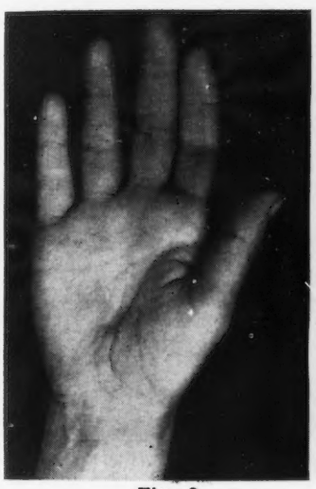

Fig. 3

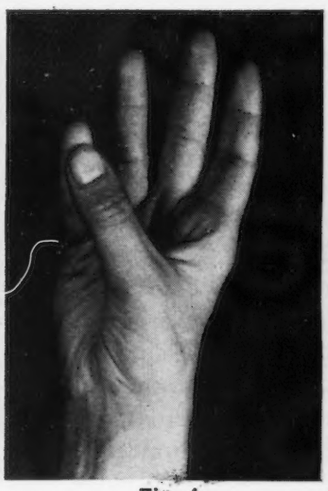

Fig. 4

Fig. 5

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Fig. 7.—"Finger tip pinch". This is the only type of pinching action that can be performed when the flexor pollicis brevis is paralyzed.

hand with the thumb pulp touching the palm at the level of the metacarpophalangeal joints (Fig. 5). The operation, therefore, should not be performed in the absence of the abductors unless their action can be replaced. There are several ways of doing this. The palmaris longus can be used as a motor. It can be sutured directly to the abductor pollicis longus, or it may be attached by a free tendon graft to the head of the first metacarpal (Fig. 6). The latter method gives a greater mechanical advantage to the tendon and also gives it a slight opposition action.

In the ordinary pinching action, the palmar surface of the thumb is opposed to the finger (Fig. 2). If the adductor pollicis is weak, much of the strength of this movement is lost and the patient reinforces the action by using the long flexor of the thumb, and by so doing flexes the interphalangeal joint of the thumb. Similarly, if the flexor pollicis brevis is paralyzed, flexion of the metacarpophalangeal joint of the thumb (which is necessary for the pinch action) is effected by the long thumb flexor. This produces flexion of both the metacarpophalangeal and the interphalangeal joints of the thumb, resulting in a "finger-tip pinch" (Fig. 7). This type of pinch action is normally employed in picking up small objects such as a pin, but it is not nearly so efficient as a grasping mechanism as the "pulp pinch" with the terminal phalanx extended.

The ability of an opponens transfer to restore a powerful pinch between the thumb and the fingers will depend partly on the strength of the short flexor and the adductor of the thumb. If the adductor and the flexor pollicis brevis are both paralyzed, the tendon transfer should be combined with fusion of the interphalangeal joint of the thumb in extension.

The ability to grasp objects between the side of the index and the thumb is dependent, not only on the ability to oppose the thumb, but also on the ability to abduct the index finger. This is particularly noticeable in the act of writing. The pen is held and controlled by opposition and the flexion of the thumb on one side, and by contraction of the sublimis tendon and abduction of the index by the first dorsal interosseous (Fig. 8). The action of the first dorsal interosseous is accentuated in such actions as making the upstroke of an "L". The importance of abduction of the index is also seen in a multitude of common hand actions, such as picking up magazines, carrying parcels, doing up buttons, or holding shoe laces.

If the first dorsal interosseous is paralyzed, opponens restitution should be combined with an attempt to restore abduction of the index finger. This can be achieved by transferring the flexor sublimis tendon of the middle finger to the first dorsal interosseous.

There is nothing much to the operative technique. A transverse skin incision is made just

Fig. 8.—When holding a pen, the index finger is powerfully abducted. Note the belly of the contracting first dorsal interosseous.

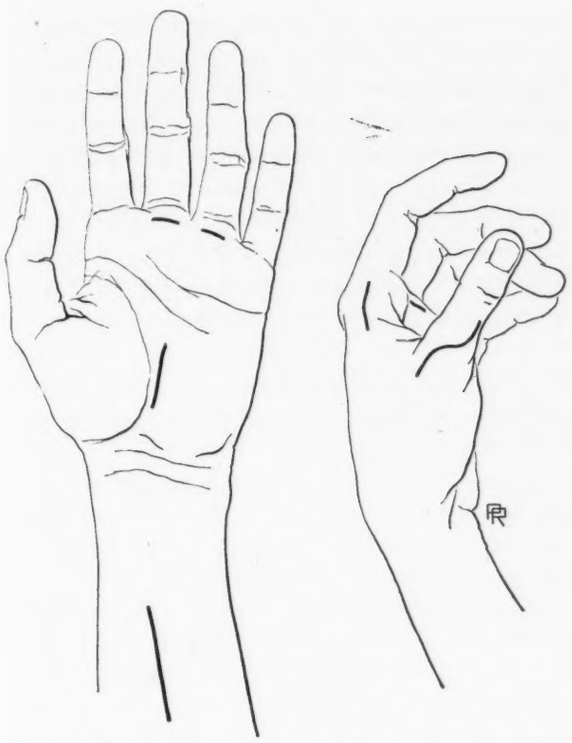

Fig. 9.—Diagram to show the site of the skin incisions commonly employed.

proximal to the digital crease; this facilitates suture (Fig. 9). If the incision is made in the crease itself, the wound edges tend to invert. Care is taken not to damage the digital nerves. The sublimis tendon is divided at the level of the proximal interphalangeal joint. If it is divided more proximally than this, the distal portion of the tendon may adhere to the proximal phalanx, giving rise to a flexion deformity of the proximal interphalangeal joint. We have had one instance of this. If it is divided distal to the proximal interphalangeal joint, it is theoretically possible to get a hyperextension deformity of the joint.

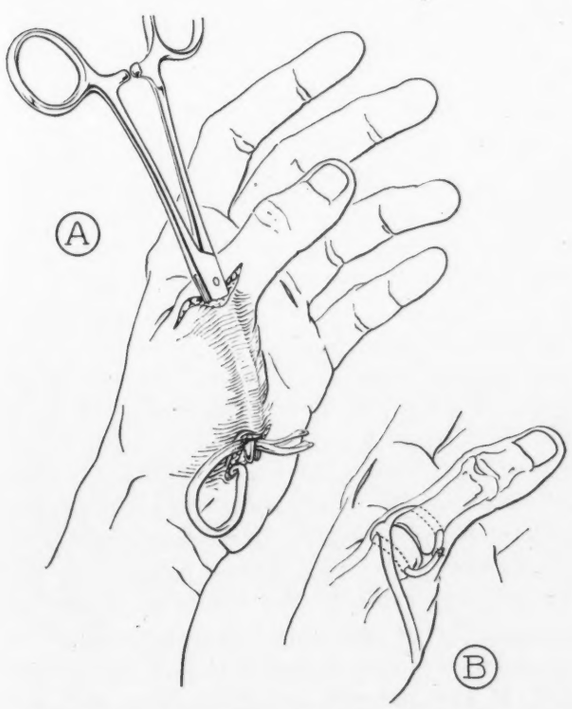

Fig. 10.—The flexor digitorum sublimis is drawn subcutaneously from the palm to the dorsum of the thumb. It is very important that this tendon lie in the subcutaneous pad. In Fig. B, the details of the suture of the tendon are shown.

A second incision is made in the palm in line with the finger, two fingerbreadths above the distal wrist crease, and the divided tendon drawn through it. A third incision in the form of a lazy S is made over the metacarpophalangeal joint of the thumb. A transverse drill hole is made through the head of the first metacarpal and through the base of the proximal phalanx. The flexor tendon is drawn through a subcutaneous tunnel from the palm to the thumb (Fig. 10). At this stage the palm incisions should be sutured, as this is a difficult feat when the thumb is held over in the full opposition necessary at the termination of the operation.

The two halves of the sublimis tendon are threaded through the drill holes and sutured on the radial side of the metacarpophalangeal joint. The details of fixation are not very important. The tendons may be sutured to each other, they may be held by buttons and a pull-out wire, or they may be sutured to the periosteum and available soft tissue. All this is a matter of the individual surgeon's preference. However, the two halves of the tendon, after they have been pulled through the drill holes in the bone, should not be sutured to the main trunk of the transposed tendon. If this is done, the pull is centred on the radial side of the joint and much of the windlass rotating action of the transfer is lost.

If the flexor sublimis to the middle finger is to be used to replace the first dorsal interosseous, the tendon is pulled out of an incision in the forearm and transferred subcutaneously across the radial border of the forearm on to the dorsum of the hand to the radial side of the base of the index, where it is sutured under tension to the insertion of the first dorsal interosseous.

At the completion of the operation, a pressure dressing is applied and the hand is then encased in a plaster mitt. At the end of 10 days, the plaster is removed, the sutures are removed and a light plaster is applied holding the thumb in

full opposition and the index finger in abduction, if the first dorsal interosseous has been replaced. This is maintained for a further two weeks, at the end of which time the plaster is removed and rehabilitation started.

SUMMARY

This operation has been used on 16 patients without a failure. Exact assessment and grading of results in patients suffering from poliomyelitis is difficult because the final outcome is dependent upon the total residual paralysis in the hand. However, the operation can transform a useless hand into one which the patient can use for everyday activities if due attention is paid to the associated muscular paralyses. The greatest virtue of this operation is its beautiful simplicity. The additional procedures that are commonly necessary are tendon transfers to replace paralyzed abductors of the thumb and the first dorsal interosseous; interphalangeal fusion of the thumb is necessary when the adductors pollicis and the flexor pollicis brevis are both paralyzed.

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THE USE OF LIPOTROPIC FACTORS IN THE TREATMENT OF ALCOHOLISM

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PHYSICIANS TREATING ALCOHOLICS, and in particular those with liver disease, are often undecided whether or not to use lipotropic substances in the treatment schedule. This study was designed to test the effects of using lipotropic factors as part of the routine treatment of patients whose constant or frequent use of alcoholic beverages has reached the stage where hospitalization is necessary. The subjects of the study were patients at Brookside Clinic, Toronto, a provincially sponsored clinic for the treatment of alcoholism, operated by the Alcoholism Research Foundation of Ontario. Approximately half of the patients admitted to Brookside Hospital have frank fatty liver (as indicated by the presence of an enlarged, firm, tender liver) or Lænnec's cirrhosis. Undoubtedly, many others have the subclinical disease. Experimental investigations with animals[1, 2] have shown that supplementary lipotropic factors are of value in the prevention of fatty liver produced by dietary deficiencies. Because of such evidence this study was undertaken to determine whether the supplementary administration of lipotropic substances would hasten the recovery of alcoholic patients from the effects of a prolonged period of excessive drinking and faulty dietary intake.

*From the Alcoholism Research Foundation of Ontario, Toronto.

METHOD

A simple randomized design was used. Consecutive admissions to Brookside Hospital were randomly assigned to an experimental and to a placebo group until the groups contained 30 and 31 subjects respectively. When all the members of the experimental and placebo groups had been discharged from the hospital, an additional group composed of 19 consecutive admissions was added to the study for comparative purposes.

Seventy of the subjects were men and ten were women. They ranged in age from 26 to 61, with a mean of 42 years. Constant or frequent excessive use of alcoholic beverages had existed in the patients for from 1 to 39 years with a mean of 12 years. The length of the pre-admission drinking bout ranged from one to 180 days with a mean of 27 days. The associated period of greatly reduced food intake was from 0 to 100 days with a mean of 15 days. All of the patients had been sober from one to three days before admission. Forty-seven per cent of the subjects were found to have fatty liver and 2% Lænnec's cirrhosis. These proportions are closely comparable to the results of an earlier investigation of 430 consecutive admissions to Brookside Hospital in which is was found that 45% of the patients had fatty liver and 2% Lænnec's cirrhosis.[3] This indicates that the present sample is representative of our patient-population with respect to liver disturbance.

Psychiatric examination of the sample revealed that, in addition to alcoholism, 46% of the subjects were suffering from recognizable personality disturbances of varying degrees of severity, 14% from psychoneurosis, and 2% from psychosis.

Statistical tests demonstrated that the three groups did not differ significantly in sex composition, age, length of established alcoholism, length of pre-admission bout, and length of period of reduced food intake.

Every effort was made to keep the data unbiased. Those who were engaged in making or recording observations or in analyzing the data did so without knowledge of which substance the subjects were receiving. The material used for study was a proprietary preparation containing choline, methionine, inositol, vitamin B_{12}, liver concentrate and desiccated liver.* The lipotropic substance and placebo capsules were identical in size, shape, colour, and smell. Two staff members not otherwise taking part in the experiment were responsible for assigning patients to the groups and for making certain that the correct substance was administered to each patient. The subjects in the experimental and placebo groups were given three capsules three times daily before meals. They were told that they were participating in an experiment to test the efficacy of a substance in hastening recovery from the effects of acute alcoholism. They were carefully instructed concerning the necessity of conscientiously taking the prescribed number of capsules daily for a 90-day period. The importance of returning to the hospital for examination on the prescribed dates was also emphasized.

The control group was given no capsules at all. With the exception of the bromsulphalein test, they were subjected to the same observations as the other two groups. Although they were asked to return for further examinations after discharge, in precisely the same way as the subjects in the other two groups, so few did so that it was not possible to obtain a sufficient amount of comparative data beyond the hospitalization period to be of any value for analysis.

Certain observations were made on each subject at the time of admission to hospital. These were repeated at the end of seven, 14, 30, 60, and 90 days. Other observations were made daily for the 14-day period that the subjects remained in hospital and at each of the three subsequent examinations. The observations made were as follows:

1. Diet and drinking immediately preceding patient's admission: A notation was made as to the length of the drinking bout immediately preceding the patient's admission and the number of days during which there was negligible dietary intake.
2. Appetite: A daily record was made for each meal as to whether all, part, or none was consumed.
3. Sleep: A daily record was made of the number of hours of sleep.
4. Well-being: This referred to the patient's subjective state of well-being. It was recorded daily (good, fair, or poor) and at each subsequent examination.
5. Pulse: Recorded daily and at each subsequent examination.
6. Respiration: Recorded daily and at each subsequent examination.
7. Temperature: Recorded daily and at each subsequent examination.
8. Blood pressure: Recorded on admission, on the seventh day, the 14th, and at each subsequent examination.
9. Weight: Each patient was weighed on admission, on the seventh day, the 14th, and at each subsequent examination.
10. Tremor: A daily record was made of the presence or absence of coarse tremor.
11. Sedation: A daily record was made of any sedatives administered and of any demands for sedation.
12. Liver size: Recorded on admission, and if the liver was enlarged, on the seventh day and at each subsequent examination.
13. A bromsulphalein retention test, a Hanger flocculation test, a thymol turbidity test, and a mercuric chloride number determination were carried out as soon as possible after admission to Brookside Hospital. If abnormal results were obtained, the tests were repeated at the time of the patient's discharge and at each subsequent examination.

All of the subjects were given a standard hospital diet during the 14-day period of hospitalization. The average daily intake per patient was approximately 400 g. of carbohydrate, 150 g. of fat, and 125 g. of protein. There were no significant differences among the groups in amount of food consumed during this time.

At the time of discharge from the hospital each patient was given a sufficient number of appropriate capsules to last him until the next observation date. When he reported for his examination at that time, he was again given a further supply to last him until the next examination.

The results were analyzed in two ways. First, an attempt was made to obtain an over-all clinical judgment concerning the number of days required by each subject to recover from the effects of his pre-admission drinking bout and associated dietary neglect. This was done by having two physicians independently exam-

*Nine capsules contain: choline dihydrogen citrate 2.5 g., di-methionine 1.0 g., inositol 0.75 g., vitamin B_{12} 18 μg., liver concentrate and desiccated liver 0.78 g.

ine the subjects' protocols and on that basis make a judgment concerning the time at which the patient had achieved a state of well-being defined in terms of his usual level of functioning. Secondly, criteria such as weight, liver size, and the results of the four liver function tests were analyzed separately, to determine whether or not any significant differences appeared between the experimental and the placebo group.

RESULTS

Table I shows that clinical recovery does not occur more rapidly in the experimental subjects than in the subjects receiving the placebo or in those receiving no capsule at all.

TABLE I.

MEAN NUMBER OF DAYS UNTIL CLINICAL RECOVERY FOR SUBJECTS GIVEN LIPOTROPIC SUBSTANCE OR PLACEBO AND CONTROL SUBJECTS

Lipotropic substance		*Placebo*		*Control*	
Mn.	*N*	*Mn.*	*N*	*Mn.*	*N*
7.4	28	5.8	29	5.8	19

A test of the significance of the difference between the mean for the experimental group and that for the placebo group yields a "t" of 1.14. The same result is obtained when the test is applied to the difference between the means for the experimental and control groups. For significance at the 0.5 level of confidence "t's" of 2.6 and 2.7 respectively would be required. The differences between the means are, therefore, not statistically significant. Table II shows that the experimental and the placebo group did not differ significantly in respect to weight on any of the observation days.

Table III shows that there is no significant difference between the proportion of experimental and placebo subjects having normal liver size on the various observation days.

TABLE III.

PROPORTION OF EXPERIMENTAL AND PLACEBO PATIENTS HAVING NORMAL LIVER SIZE ON OBSERVATION DAYS

Observation day	*Experimental*		*Placebo*		*Chi-square*
	No.	*%*	*No.*	*%*	
1st	17	56.7	15	50.0	.067
14th	17	73.9	14	58.3	.671
30th	15	75.0	15	71.4	.009
60th	13	92.9	10	76.9	.387
90th	8	88.9	8	80.0	.010
with 1 d.f. $X^2_{.05}$		=3.841			

Tables IV, V, VI and VII show that there is no significant difference between the proportion of experimental and placebo subjects having normal liver function test results on the various observation days.

Table IV shows that the proportion of experimental and placebo subjects having normal bromsulphalein retention does not differ significantly on any of the observation days.

TABLE IV.

EXPERIMENTAL AND PLACEBO SUBJECTS HAVING NORMAL BROMSULPHALEIN TEST RESULTS ON OBSERVATION DAYS

Observation day	*Lipotropic substance*		*Placebo*		*Chi-square*
	No.	*%*	*No.*	*%*	
1st	14	50	16	61	.335
14th	19	73	24	92	2.149
30th	17	81	20	100	.234
60th	11	85	13	100	.542
90th	9	100	8	100	—
with 1 d.f. $X^2_{.05}$		=3.841			

Table V shows that the proportion of experimental and placebo subjects having normal results on Hanger flocculation tests does not differ significantly on any of the observation days.

TABLE II.

MEAN WEIGHT FOR EXPERIMENTAL AND PLACEBO SUBJECTS ON OBSERVATION DAYS

Observation day	*Lipotropic substance*		*Placebo*		*Obtained "t"*	*"t" required for significance at the .05 level of confidence*
	Mn.	*N*	*Mn.*	*N*		
1st	157	29	151	29	1.14	2.6
14th	161	29	155	29	.86	2.6
30th	157	21	153	21	1.48	2.7
60th	166	13	146	14	1.79	2.7
90th	164	10	152	9	.92	2.9

TABLE V.

EXPERIMENTAL AND PLACEBO SUBJECTS HAVING NORMAL HANGER FLOCCULATION TEST RESULTS ON OBSERVATION DAYS

Observation day	*Lipotropic substance*		*Placebo*		*Chi-square*
	No.	*%*	*No.*	*%*	
1st	20	69	21	72	——
14th	23	82	22	85	.015
30th	18	82	16	84	.005
60th	12	92	10	77	.295
90th	9	90	7	87	.344
with 1 d.f. X^2 .05	=3.841				

Table VI shows that the proportion of experimental and placebo subjects having normal results on the thymol turbidity test does not differ significantly on any of the observation days.

TABLE VI.

EXPERIMENTAL AND PLACEBO SUBJECTS HAVING NORMAL THYMOL TURBIDITY TEST RESULTS ON OBSERVATION DAYS

Observation day	*Lipotropic substance*		*Placebo*		*Chi-square*
	No.	*%*	*No.*	*%*	
1st	8	27	10	34	.136
14th	9	31	12	44	.577
30th	12	57	12	67	.780
60th	10	77	10	77	——
90th	8	80	6	75	.100
with 1 d.f. X^2 .05	=3.841				

Table VII shows that the proportion of experimental and placebo subjects having normal results on the mercuric chloride test does not differ significantly on any of the observation days.

TABLE VII.

EXPERIMENTAL AND PLACEBO SUBJECTS HAVING NORMAL MERCURIC CHLORIDE TEST RESULTS ON OBSERVATION DAYS

Observation day	*Lipotropic substance*		*Placebo*		*Chi-square*
	No.	*%*	*No.*	*%*	
1st	21	72	25	86	.946
14th	23	82	25	93	.574
30th	19	86	19	95	.181
60th	12	92	13	93	.463
90th	9	90	6	67	.465
with 1 d.f. X^2 .05	=3.841				

DISCUSSION

The results show that the supplemental administration of lipotropic factors to a sample of alcoholic patients did not appear to hasten their recovery, as measured by the criteria of this study. The diet consumed by these patients while in hospital contained adequate amounts of these substances and there is no reason to believe that an excess of lipotropic factors is of value. Best *et al.*[4] have shown that two types of fatty liver may be produced in experimental animals. The first type is associated with a deficiency of lipotropic factors and is prevented by the administration of these substances. In this type the fat deposits are around the central veins of the hepatic lobules. The second type is associated with protein malnutrition and is relieved by administration of protein but not of choline. In this type the fat is deposited around the portal tracts. There is some evidence to suggest that the fatty liver developing in alcoholics may be of the second variety.[5] If this is true, and if a diet contains an abundance of lipotropic agents, then one would not expect the supplemental administration of these substances to exert a marked beneficial effect.

CONCLUSIONS

The administration of lipotropic factors to alcoholic patients of the type described in this paper does not appear to hasten their recovery from the effects of a prolonged period of excessive drinking and faulty dietary intake.

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LEARNING AND STATISTICS

"A capacity to learn is the diagnostic character of brain, and the hypothesis that a learning brain is perpetually scanning the world of experience for statistically significant information suggests a fresh experimental approach to the problem of how animals learn . . . It looks very much as though an animal—human or otherwise—in a learning situation is acting as if it were a statistical computer set to accept, as significant, odds greater than 1,000 to 1 against chance association. If the basis of learning is the computation of contingency, then most animals are considerably more sceptical than professional statisticians, who generally consider odds of 100 to 1 against chance as indicating significance."—W. Grey Walter, *Nature*, 177: 685, 1956.

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CARDIAC ARREST—CAUSATION AND MANAGEMENT*

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DURING THE PAST FOUR or five years many cases of cardiac arrest have been reported in the literature, some with discussion of the cause, but many reported as isolated incidents in a busy hospital operating room. Parallel to this has been the development of hypothermic anæsthesia with its concomitant risk of cardiac arrest. With the increased interest in this complication there have been many efforts to produce some sort of electrical control of the heart, both by defibrillation and use of an electrical pacemaker. The machine used at Westminster Hospital was designed by the National Research Council of Canada, Radio & Electrical Engineering Division, and manufactured by Measurement Engineering Ltd. (Stimulator-defibrillator Model 1033).

This paper deals with sudden standstill or fibrillation of the heart occurring in the operating room. It does not include accidents associated with hypothermic techniques nor does it propose to cover every phase of this vast subject of arrest. It is intended to give a brief review of cardiac physiology, to list some of the causes of cardiac arrest, to offer a method of resuscitation, and to describe the use of the stimulator-defibrillator available in this hospital.

Cardiac muscle exhibits three main properties: (1) excitability and contractility; (2) rhythmicity; (3) conductivity. If a stimulus is great enough to cause the heart muscle to contract, the impulse will spread so that the maximum possible contraction will be produced. This is called the "all or none" law. The actual period of contraction is the only time during which the heart muscle will not respond to another stimulus. It is the absolute refractory period. The total period of relaxation is the relative refractory period. At the beginning of this interval a large stimulus will produce a relatively weak contraction. Later on in the period of relaxation when the heart has regained more of its resting charge a small stimulus will produce a much better contraction. Cardiac muscle contracts rhythmically. Even the isolated heart specimen will not hold a sustained contraction but beats intermittently. Heart muscle is composed of a type of striated muscle which has no sarcolemma or insulating sheath. The fibres are joined together by protoplasmic bands to form a continuous network or syncytium. When the muscle is stimulated in any one area, the impulse travels along these branching fibres to involve the whole muscle.

In the human heart there is a specialized tissue called junctional tissue which originates and conducts impulses much faster than the muscle fibre. This is composed of primitive muscle cells, nerve cells and nerve fibres. The first part is the sino-auricular (S-A) node, about 3-4 cm. long, located in the right auricle at the base of the superior vena cava. It is here that the cardiac impulse originates, and it is often called the pacemaker of the heart. The excitation wave travels radially from the S-A node in the auricular muscle until it reaches the auriculo-ventricular (A-V) node, at the top of the interventricular septum. From the A-V node a bundle of conducting tissue extends down through the interventricular septum. This is known as the A-V bundle or bundle of His, and divides into two branches, one going to each ventricle. The branches divide repeatedly in the area under the endocardium to form the Purkinje network. Impulses will travel at the rate of 500 mm. per second in the heart muscle fibre but at the rate of 5,000 mm. per second in the junctional tissue.

The cardiac cycle is most easily picked up at the period just following ventricular systole. This period of ventricular relaxation is divided into four parts:

1. The isometric relaxation—the heart muscle fibre has not yet begun to lengthen. This lasts for about 0.06 sec. and is terminated by the opening of the A-V valves.

2. The period of rapid filling or diastolic inflow: The blood from the auricles rushes into the ventricular cavity. This takes about 0.1 sec.

3. The period of diastasis: The blood flow from the auricle into the ventricle is very slow and almost ceases. Any change in heart rate usually occurs at the expense of this period.

4. Auricular systole: The auricles then actively discharge their contents into the ventricular cavity for a period of 0.1 sec.

Auricular systole is followed immediately by ventricular systole. This too is divided into sec-

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tions: First—the period of isometric contraction. The ventricular muscle begins to contract on its load of blood, immediately closing the A-V valves. The ventricle must then produce a pressure head in the cavity great enough to overcome the diastolic pressures of the pulmonary and systemic circulations. When this is reached, the pulmonary and aortic valves open and the period of ejection is begun. This period of ejection lasts about 0.3 sec.

The electrocardiogram is a written record representing the summation of electrical potentials present in the heart muscle at any given time. The P wave begins with the excitation of the S-A node and indicates the beginning of auricular contraction. The QRS group represents the depolarization and therefore the contraction of the ventricular muscle. The T wave is produced by the repolarization of the ventricular muscle.

The last topic in cardiac physiology will be a brief mention of some arrhythmias. Extrasystoles can be of three types—auricular, nodal and ventricular. The auricular extrasystole arises in some part of the auricular muscle other than the S-A node. The extra impulse will produce a complete cardiac cycle of probably weaker strength than a normal beat. The pacemaker sends off its impulse at the regular time with no reference to the beat from the ectopic centre. In the nodal type, an impulse originates in the A-V node and travels both up and down, causing contraction of the auricle and ventricle almost simultaneously. The last is the ventricular extrasystole and is the most important to us. The ectopic centre is anywhere in the ventricular muscle and the impulse is initiated during the normal relaxation period of the ventricle. The ventricle then contracts. If the normal pacemaker stimulus finds the ventricular muscle in the absolute refractory state, no further excitation can occur. The ventricular muscle then relaxes and stays in this state until the next normal impulse from the pacemaker produces the regular ventricular contraction. Therefore, a compensatory pause nearly always follows the ventricular premature beat. The patient may have a run of these extrasystoles of any of the three types causing paroxysmal tachycardia. Ventricular tachycardia if rapid enough may develop into ventricular fibrillation. In fibrillation small areas of muscle have established their own rhythm of contraction. The picture is one of generalized inco-ordinate activity. There is no one stimulus in the muscle mass strong enough to produce active contraction of the chambers involved great enough to do work.

ELECTRICAL DEFIBRILLATION

Now, in experimental stimulation of canine hearts, it was found that a weak current could produce ventricular fibrillation and a stronger current could stop it. Therefore, the whole principle behind the electrical defibrillator is to produce a current strong enough for a period of time great enough to produce a contraction of all components of ventricular muscle. The ventricular muscle then enters its relative refractory period as a unit. A second stimulus given to the ventricular muscle during this refractory period allows the ventricular muscle to contract as a whole and accomplish work.

The countershock defibrillator has three main components: (1) a sinusoidal current; (2) a voltage control and therefore a control of the current used; (3) a switch to control the duration of current. In our defibrillator an automatic timer in the foot switch eliminates any guesswork on the part of the operator. Every time the foot switch is tripped one shock is produced, and the foot switch must then be released before another shock can be given. This machine is operated on a 60-cycle current. A switch just inside the cover allows for setting the timer at 8-12 or 16 cycles of the 60-cycle current or equivalent to 0.13-0.2 and 0.25 sec. The voltage control is also inside the cover and can be set at 170 or 220 volts. The amperage is constant at 1.6 amps. The electrodes are circular and concave and by experiment have been found to have an optimum diameter of 2½ inches. The procedure in the use of the defibrillator is simple.

1. The machine is switched on, and left in this position for about three minutes. The red light glows, showing that the condenser system is charging.

2. The electrodes are dipped in saline or covered with saline gauze and placed in an antero-posterior position on the heart.

3. It is probably wise to set the machine at the lowest current of 170 volts and the shortest time of 0.13 sec. for the initial shock.

4. The main switch is then turned to defibrillation and the setup is ready.

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5. When the foot switch is tripped, the current flows through the heart and the white light flashes for the duration of the current.

6. If a single shock does not stop the fibrillation, a series of 5-10 single shocks at ½-second intervals can be tried. If the heart is still fibrillating, the hand massage should be started again for a short period and the duration of current increased. If fibrillation cannot be stopped on any one of the three time settings, the voltage can be raised to 220 volts and the process repeated. I might add here that shocks of 0.1 to 0.2 second duration do not appreciably alter cardiac resistance. However, shocks of a longer duration tend to lower resistance and therefore increase the current flow, with a danger of thermal damage and necrosis of muscle.

CAUSES OF CARDIAC ARREST

The common denominator in nearly all cases of cardiac arrest is anoxia. This state produces some degree of heart damage and therefore a myocardium more susceptible to other factors which might cause injury. Anoxia may be divided into four main groups:

1. Anoxic, in which the oxygen tension of the blood is decreased.

2. Stagnant, in which the blood flow is so slow that the blood has lost more than its share of oxygen.

3. Anæmic, in which the Hb content of the blood is not adequate to carry sufficient oxygen.

4. Histotoxic, in which some derangement of tissue metabolism does not allow use of the oxygen carried to it.

In cardiac arrest we are concerned with the anoxic type, very frequently with the anæmic type if there has been any great degree of hæmorrhage, and certainly with the stagnant type after the accident has occurred.

The second main factor is vagal stimulation. The cardiac vagal nerves end in auricular tissue only: the right vagus goes to the S-A node and the left vagus to the A-V node. Stimulation produces bradycardia and hypotension. If the stimulus is great enough, cardiac standstill is produced. There are various groups of vagal stimulation:

1. Craniocardiac: With these the afferent loop of the arc comes from the head and neck through a cranial nerve and the efferent loop is the cardiac vagus. Examples are: (a) nasal mucosal stimulation carried through the trigeminal nerve; (b) pressure on the outer part of the eyeball stimulating the so-called oculocardiac nerve, through the oculomotor; (c) the carotid sinus reflex carried through the glossopharyngeal nerve.

2. Vagovagal reflexes: The respiratory system is richly supplied with vagal nerve endings. Stimulation of the larynx, trachea, or particularly the carina may set up an afferent arc with efferent arc to the heart.

3. Rectocardiac: The sacral outflow of the parasympathetic supplies the rectum and anal canal. Operative interference in this area under too light anæsthesia may produce reflex cardiac arrest. The efferent loop may also be to the larynx and cause laryngospasm.

4. Direct stimulation of the vagus during operative procedures should for the most part be avoided. Moderate stimulation of the nerves in the neck might produce bradycardia, whereas the same stimulation lower down and particularly at the level of the heart might be severe enough to produce arrest. As the point of stimulus travels down toward the abdomen, the vagal effect decreases. Therefore, during bilateral vagotomy, the nerves should be sectioned as low as possible to produce little or no effect.

5. The pericardium is richly supplied with vagal endings and any manipulation has a pronounced effect.

6. During high spinal anæsthesia the cardiac sympathetic nerves may be blocked, leaving a preponderance of vagal tone with bradycardia.

Other causes of cardiac arrest are: (a) Direct trauma to the heart or pericardium. (b) The effect of anæsthetic agents. All anæsthetics are cardiac poisons, some more potent than others, and deep anæsthesia always carries this danger. Also most of the anæsthetic agents we use are cholinergic; that is, they produce acetylcholine which enhances the already present vagal tone. This is spoken of as sensitizing the muscle to any vagal stimulation.

There are, of course, other reasons for arrest due to definite organic damage, such as coronary occlusion, pulmonary embolus, and cerebral vascular accident.

CARDIAC RESUSCITATION

We would like to outline a working method of cardiac resuscitation; there are many such routines but the essence of all is immediate diagnosis and fast team-work. According to the literature, cardiac arrest occurs in one in 5,000-7,000 cases in a busy centre. There is a period of about three minutes in which the circulation must be restored or there will be some degree of cerebral damage. This time is further reduced by the degree of anoxia present at the time of the arrest, and the 30 seconds taken by the anæsthetist and the surgeon to diagnose the condition. Therefore, begin cardiac massage immediately and worry about restoring the heart beat later.

The best results from cardiac resuscitation are obtained in persons with good hearts, good lungs and an adequate blood volume. There are two main aims: to restore the oxygen system and to restore the circulation. One is of no use without the other. The brain must be supplied with oxygenated blood under adequate pressure.

As soon as the accident occurs and a definite diagnosis is made: (1) The anæsthetist places the patient in 15° Trendelenburg position, stops all anæsthetic agents, and gives the patient 100% oxygen under positive pressure. The patient is intubated at the earliest possible convenience. (2) An intravenous drip is set up. If fibrillation is present, a solution of 0.1% procaine is started. (3) During this time some other person is taking serial readings of blood pressure. (4) Someone is calling out the time every 30 seconds. (5) In the case of cardiac standstill the anæsthetist gives the patient 1/50 grain atropine intravenously as soon as possible to counteract vagal stimulation. (6) The surgeon has his own duties while this is going on. Hand massage should be started immediately whether the heart is in standstill or fibrillation. An easy approach is by an incision through the fifth left interspace. The ribs are spread with the rib spreaders and the hand is inserted. Massage should be carried on at a rate—usually 50-60 times a minute—compatible with adequate filling of the ventricle. (7) Another surgical team should scrub up immediately. Cardiac massage is tiring work and one operator cannot carry on for long. (8) If the systolic B.P. is not up to 80 within one minute of starting massage, a cut-down on the radial artery should be done by the surgical team and blood or Subtosan given under pressure.

Fig. 1

When these things are accomplished, the patient is out of danger. Now remains the assessment of the heart and the restoration of the beat. The heart stops in either standstill or fibrillation. The accepted treatment of cardiac standstill is the injection of 0.5 c.c. of 1:1,000 adrenaline diluted to 5 c.c. with normal saline directly into the presenting surface of the heart. This will probably be the right ventricle. Some authorities say that a heart in standstill will always commence beating with adrenaline. Ventricular fibrillation is diagnosed by direct observation of the heart or by E.C.G. If fibrillation is present, the heart should be sprayed with or have injected into it 5 c.c. of 1% procaine. The heart is then defibrillated by the countershock defibrillator as described before. The heart is shocked into standstill, which is then treated with adrenaline. Other drugs are of questionable value. Some use $CaCl_2$; others advocate heparin.

There are, of course, all grades of recovery after cardiac massage. These can be divided into three main groups: (1) Complete recovery of cardiac, respiratory, and cerebral function. (2) Permanent recovery of heart beat and respiratory function, but little or no recovery of cerebral function. These people may live for years. (3) Recovery of heart beat but no recovery of respiratory or cerebral function. These people die within hours of the accident.

After the great flurry is over, a decision must be made whether or not to continue with the original operation. If the patient is young and healthy and it is an emergency operation, the surgeon is quite justified in going ahead even

if the accident occurred before the incision. If it is an elective procedure, it might be well to postpone operation.

There are just a few points in the post-emergency treatment.

1. The patient is left intubated until conscious. An oxygen tent is used in the recovery room if necessary.

2. If respiration does not return within a reasonable time, a respiratory may be used.

3. Any stimulant such as caffeine or Coramine may be given.

4. If the pulse is very rapid, the patient may receive quinidine or digitalis.

5. The blood pressure is maintained with blood or vasopressors.

6. A Foley catheter is placed in the bladder for easier nursing care.

ELECTRICAL STIMULATION OF THE HEART

Sometimes a heart in standstill will not commence beating with massage or with adrenaline. It is in cases of this sort that the electrical stimulator may be used. The stimulator electrode consists of two wires in a French intracardiac catheter. These wires can be up to 3 mm. apart. This electrode may be applied on the outer surface of the heart in the area of the pacemaker, or on the inner surface threaded through the jugular vein into the right auricle. For intracardiac stimulation the electrode may be placed anywhere in the upper part of the right auricle and still produce effective excitation. If the electrode is too far into the auricle, the phrenic nerve will be stimulated and the diaphragm will contract. When the pacemaker is stimulated, a complete cardiac cycle is produced, as is proven by E.C.G. recordings. The heart rate can be controlled at much higher than normal values but only at 15-20% lower than normal rates. At these lower rates the heart tends to "escape" from electrical control and produce spontaneous extrasystoles. During this period of electrical control the blood pressure can be maintained within normal limits. It is to be hoped that when the artificial stimulus is removed the heart will continue to beat at a rate governed by the dynamics of the system.

To use the stimulator, turn the central knob to STIM. LOW position. This disconnects the defibrillator circuit immediately. The timer device is the pulse rate dial and is set at some value slightly higher than the patient's average pulse rate. The voltage regulator is the dial on the left. When the central knob is set at STIM. LOW the numbers on the dial represent 0.5-1-1.5, etc., volts. In the STIM. HIGH position the numbers represent 5-10-15, etc., volts. The pulse stimulation has a duration of about 4 milliseconds. When the electrode is in the right place, the heart is stimulated with gradually increasing voltage until a contraction of the heart is produced. Any contraction of this muscle is a maximum contraction and therefore no higher voltage need be used.

SUMMARY

A brief outline of some cardiac physiology has been given and frequent causes of cardiac arrest have been reviewed. The outline given for cardiac resuscitation is essentially that proposed by Ripstein and Miller and now in active practice at the Royal Victoria Hospital, Montreal.

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RAUWOLFIA-EPHEDRINE THERAPY

Two very ancient drugs from Asia, rauwolfia and ephedrine, have now been combined for use as a hypotensive and tranquillizing agent. It had been noted that of 68 patients treated with rauwolfia preparations alone, 20 developed some untoward side-effect as a result of smooth muscle stimulation, vasodilation or mental depression. When 8 mg. of ephedrine was added to 100-200 mg. of whole powdered rauwolfia root or to 0.1-0.25 mg. of reserpine, and the combined dose given three times a day, the side-effects of the rauwolfia were eliminated, while the hypotensive effects remained.—Feinblatt *et al.*, *J. A. M. A.*, 161: 424, 1956.

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CARCINOMA OF THE LUNG
A REVIEW OF 252 CASES*

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A REVIEW of the literature over the past decade emphasizes the importance of lung cancer as a clinical entity. The authors have been interested for some time in this disease and its surgical management.

This report is based on cases seen at Shaughnessy Veterans Hospital, Vancouver General Hospital, and St. Paul's Hospital, Vancouver, B.C. The purpose of this paper is to review the end results on clinically inoperable cases, and then to discuss in some detail the results of surgical resection.

A total of 252 proven primary lung carcinomas were seen. The management of the cases and the more pertinent findings are outlined below.

Table I shows the total number of carcinomas seen and their subsequent management. Of the 252 carcinomas seen, 149 (59.1%) were accepted for surgery and of these 67.2% were resectable.

TABLE I.

MANAGEMENT OF 252 CASES

Clinically inoperable	*Thoracotomies*	*Resections*
103 (40.9%)	49 (19.4%)	100 (39.7%)

PATHOLOGY

In our series of resections four recognized types of carcinoma were found. The histological types are tabulated in Table II.

TABLE II.

HISTOLOGY AS FOUND IN 100 RESECTIONS

Cell type	*Number in 100 resections*
Squamous cell	52
Anaplastic	31
Adenocarcinoma	16
Alveolar cell	1

It is always of interest to know the survival periods in clinically inoperable cases. Table III gives a short résumé of the findings in our series.

TABLE III.

AVERAGE SURVIVAL PERIOD IN NON-RESECTABLE CASES.

Number	*Distribution*	*Average survival period*
103	Clinically inoperable	3.3 months
49	Thoracotomies	7.1 months

It is evident that the survival period for the inoperable cases is indeed brief. Patients deemed suitable, when first seen, for thoracotomy live about twice as long as those judged clinically to be inoperable. The reason presumably is that cases accepted for thoracotomy are less advanced. From the above, it is clear that the prognosis is hopeless when resection is impossible. The remainder of the paper will deal with the results in cases in which a resection was possible.

A total of 100 resections will be considered. These have been derived from the period 1946 to July 1954. Thus the postoperative follow-up period varies from 6 months to 9 years, the present status in all cases being computed on the status of each case on April 30, 1955.

All resections have been put into one of two groups: (a) 66 cases in which resection took place before April 30, 1952; (b) 34 cases in which resection took place after April 30, 1952. The separation of the resections into these two groups makes it possible to present a follow-up of three or more years in the cases in group (a).

SURGICAL MORTALITY

We include in the surgical or operative mortality all deaths occurring during the first 72 hours after operation and all deaths resulting from the complications of operation during the first 30 days. Such complications include atelectasis of the other lung, pneumonia, cardiac failure, and bronchopleural fistula.

By the above criteria, the surgical mortality is 13 deaths in 100 resections. It must be pointed out that this surgical mortality of 13.0% includes all cases, and therefore many palliative resections with no hope of cure.

At this point, two very significant classifications will be introduced. The first is "resection for cure" and it includes those cases in which no secondaries were found microscopically in the regional lymph nodes and a stump of one centimetre or more of microscopically normal bronchus could be obtained proximal to the

*Read in part before the British Columbia Surgical Society annual meeting held at Harrison Hot Springs, April 21-23, 1955.

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tumour. The second classification is "resection for palliation" and includes all cases in which secondaries were found in the regional lymph nodes or a normal bronchial stump of 1 cm. could not be obtained.

When the surgical mortality is computed on the basis of resection for cure and resection for palliation, the results are as listed in Table IV.

TABLE IV.

SURGICAL MORTALITY COMPUTED ON BASIS OF TYPE OF RESECTION IN A SERIES OF 100 RESECTIONS.

Number of resections	*Type*	*Deaths*
47	Resection for cure.....	4 (8.5%)
53	Resection for palliation.....	9 (17.0%)

The cause of death in the resections for cure in Table IV is shown in Table IVa.

TABLE IVa.

FOUR SURGICAL DEATHS IN RESECTION FOR CURE

Case number	*Period alive after resection*	*Cause of death*
Case 1	4 hours	Surgical shock
Case 2	3 days	Pulmonary œdema
Case 3	30 days	Lobar pneumonia
Case 4	30 days	Congestive heart failure

From Table IV it is seen that the majority of surgical deaths occurred in the group resected for palliation. This fact is not too surprising when one considers that palliative resections include cases with no hope of cure and also those with the bronchial stump invaded by carcinoma, thus preventing normal healing of the bronchus.

When cure rates are considered, a survival period of five years after resection is frequently quoted. From this it is understood that patients surviving for five years after a resection and clinically free of recurrence are probably cured. In our series there are 49 patients who were resected five or more years ago. Table V summarizes the results.

Analysis of all the deaths in the 49 resections five and more years previously shows that 8 were surgical deaths, 29 from extension of carcinoma, and 4 from causes other than recurrence of carcinoma. Of the latter, 1 died of pulmonary œdema three years after resection and clinically was free of recurrence of carcinoma. The remaining 3 patients died of coronary thrombosis—one at 4 years and two at 4½ years after resection; two were examined at autopsy and found to be free of recurrence and the third had shown no clinical evidence of recurrence. Thus we have 2 cases free of carcinoma at autopsy over three years after resection. Certainly one is tempted to consider them probably cured. If this is done, the cure rate in this series is raised to 10 cases out of 49 or 20.4%.

TABLE V.

49 CASES RESECTED FIVE AND MORE YEARS

Period after resection	*No. alive and clinically free of carcinoma*	*Dead of extension of carcinoma*	*Dead of other causes*
1 year	21 (42.8%)	20 (40.8%)	8
2 years	12 (24.5%)	29 (59.2%)	0
3 years	11 (22.4%)	29 (59.2%)	1
4 years	10 (20.4%)	29 (59.2%)	1
5 years	8 (16.3%)	29 (59.2%)	2

In reviewing Table V one is struck by the fact that the deaths from extension of carcinoma occurred during the first two years after resection and fully 68.9% occurred during the first year. In our series of 49 resections five and more years previously, we found that when recurrence appeared it did so within two years of resection. Thus one may surmise from this series that survival for two years after resection if the patient is clinically free of evidence of recurrence indicates potential cure. However, in view of the relatively small series, for statistical purposes we consider that a two-year period is somewhat too short on which to base probable cure. Accordingly we have chosen the period three years after resection as the index of cure.

TABLE VI.

66 CASES RESECTED THREE AND MORE YEARS

Period after resection	*No. alive and clinically free of carcinoma*	*Dead of extension of carcinoma*	*Dead of other causes*
1 year	36 (54.5%)	20 (30.3%)	0
2 years	15 (22.7%)	41 (62.1%)	1
3 years	14 (21.2%)	41 (62.1%)	1

All resections done more than 3 years previously are considered in one group. In this series we have 66 resections and we again suggest that those who at the end of three years are clinically free of recurrence of carcinoma are probably cured. Table VI shows that three years after resection 21.2% of a series of 66 patients were alive and clinically free of carcinoma. We have shown previously in our five-year resections that carcinoma did not reappear later than two years after resection. We then suggested that patients surviving for three years after resection without evidence of recurrence are probably cured. In Table VI we have 21.2% surviving for three years after resection and so may consider them probably cured. Two patients are listed as dying from other causes. The first death occurred two years after resection, with a clinical diagnosis of cardiac failure and no clinical evidence of recurrence of carcinoma. However, an autopsy was not performed, so that we cannot definitely state that the patient was free of recurrence of carcinoma. The second death occurred at three years, the clinical cause being pulmonary œdema, and no evidence existing of recurrence of carcinoma, but again there is no confirmatory autopsy.

Earlier in the paper we introduced the terms "resection for cure" and "resection for palliation". It seems advisable to repeat our definitions here when we are reviewing the survival periods in these groups. "Resection for cure" includes those cases in which no secondaries were found microscopically in the regional lymph nodes, and a stump of 1 cm. or more of microscopically normal bronchus could be obtained proximal to the tumour. "Resection for palliation" includes all cases in which secondaries were found in the regional lymph nodes or where a normal bronchial stump of 1 cm. could not be obtained.

It will be noted that this differs considerably from the usual definition of palliative operations, since it includes many cases that did not appear to be hopeless at the time of operation but in which the pathologist's report later made it apparent that complete removal of all carcinomatous tissue might not have been obtained.

TABLE VII.

66 RESECTIONS OVER THREE YEARS

Resection for cure	*Probable cures (clinically free of recurrence after 3 years)*	*Resection for palliation*	*Probable cures (clinically free of recurrence after 3 years)*
29	14 (48.3%)	37	0

In reviewing Table VII a most startling fact is noted, namely, the importance of whether a resection is one for cure or palliation. We find that, if only a resection for palliation is possible, the three-year probable cure rate is nil, whereas with resection for cure 48.3% of patients are alive and clinically free of recurrence after three years.

Of the 37 patients who had resections for palliation, the average survival period was twelve months. Two patients lived beyond two years; none was alive after three years.

Important as the type of resection is, the significance of the histological findings must not be overlooked. Earlier we mentioned that four types of lung carcinoma were found in our series of resections. The prognosis in resections based on the cell type in conjunction with the type of resection is shown in Table VIII.

TABLE VIII.

29 RESECTIONS FOR CURE OVER THREE YEARS.

Number	*Histological Type*	*Probable cures (clinically free of recurrence after 3 years)*
23 (79.3%)	Squamous cell	12 (52.2%)
4 (13.8%)	Anaplastic	1 (25.0%)
2 (6.9%)	Adenocarcinoma	1 (50.0%)

Only three types of carcinoma are considered, as the only alveolar cell carcinoma was resected one year ago and death ensued within three months of resection.

SUMMARY AND CONCLUSIONS

A series of 252 cases of primary carcinoma of the lung have been reviewed and the findings presented. Patients who survive for a period of three or more years after resection without evidence of recurrence are probably cured. Patients who have had a resection for cure have a 48.3% chance of survival for three years or more. Resection for palliation offers no chance of a cure.

A review of the over-all picture of lung cancer suggests that early diagnosis and early surgical treatment are the major factors in improving the cure rate.

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POSTOPERATIVE COUGH AND THE PROPHYLACTIC USE OF BRONCHODILATORS

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DURING THE PAST 50 YEARS, references to postoperative respiratory complications have become increasingly numerous and the varying causes put forth by different writers indicate that the problem is not a simple one.

Scott and Cutler[1] were the first to postulate the theory that they are initiated by a reflex bronchospasm. Westermark[2] and De Takats[3] found that somatic pain can cause bronchoconstriction. Xalabarder[4] demonstrated an interalveolar muscular plexus and stated that abnormal constriction of these muscles can produce atelectasis. Lucas[5] noted reflex bronchial spasm from traction on the stomach and the splanchnic plexus.

Acting upon this theory, we decided to employ bronchodilator drugs in a series of appendectomies and herniotomies, because these are common operations and have a comparable cough incidence, as is shown by Table I.

TABLE I.

Operation	*No. of cases*	*Incidence of cough*	*Percentage*
Laparotomy (upper)	461	93	21.7
Thyroidectomy	55	8	14.5
Herniotomy	812	112	13.7
Laparotomy (lower)	1,478	153	10.3
Appendectomy	1,100	112	10.0
Nephrectomy	51	3	5.9
Miscellaneous	2,139	31	1.4
Orthopædic	1,990	27	1.3
Urogenital and anal	3,256	32	1.0
Ear, nose and throat	2,360	16	0.7
Ophthalmic	401	1	0.2
Total	14,103	588	4.9

In this series every cough, however slight, has been recorded, except cases with a preoperative cough not increased by the operation.

The agents selected for this trial were: theophylline ethylenediamine, given systematically, and N-isopropyl-noradrenaline, given by aerosol inhalation.

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In 1940, Gilbert and Goldman,[6] using sections of lungs from puppies in which constriction had been produced by histamine, found that theophylline ethylenediamine 1:1,000 caused a dilatation of 100% of the normal area. Young and Gilbert in 1941[7] established that this drug in the same concentration had a definite protective activity against the constrictive action of histamine. They demonstrated also that it reduced the mortality due to histamine from 80% to 56% in the guinea-pig. They believe that the action is a local one. Luduena in 1942[8] saw that theophylline ethylenediamine prevented or relieved bronchospasm in the isolated lung of guinea-pigs. Compared with adrenaline it is not only effective, but also longer lasting. He concluded that it acts by directly depressing bronchial smooth muscle. Green, Paul and Feller in 1937[9] found that the vital capacity increased in 9 out of 11 patients with asthma.

Van Heerswynghels in 1937[10] stated that theophylline ethylenediamine injected intravenously into anæsthetized dogs produces an immediate increase in rate and amplitude of respiration. When the respiration has been rendered periodic by intravenous morphine or hexobarbitone, this drug restores the rhythm; because it acts within two seconds from the end of the injection, he deduced that it exerts its action on the respiratory centre by chemical stimulation. Denervation of the carotid sinus does not abolish this action. Marais and McMichael[11] found that theophylline ethylenediamine stops Cheyne-Stokes respiration for up to 24 hours, and attributed this fact to direct stimulation of the respiratory centre. Green, Paul and Feller[9] on the other hand thought that this was only due to improved cerebral circulation, because they demonstrated a fall in venous pressure coinciding with a fall in intracranial pressure. Every worker who has studied the action of theophylline ethylenediamine on the coronary circulation has found that it brings about vasodilatation; Smith, Miller and Graber in 1925[12] demonstrated that in the isolated heart of the rabbit, coronary flow was increased by 40% to 90%, a rise comparable with that caused by nitroglycerin. Lindner and Katz[13] believe that it acts directly on the coronary vessels.

N-isopropyl-noradrenaline was synthesized in Germany and is very acid and highly soluble in water. Konzett in 1940[15] demonstrated experimentally that N-isopropyl-noradrenaline, as a

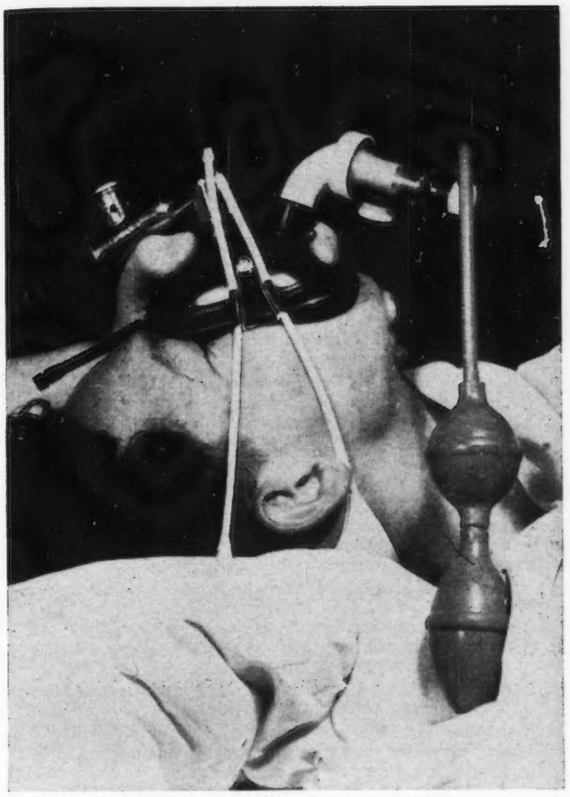

Fig. 1

bronchodilator, is 10 times as potent as adrenaline and that it acts peripherally on the bronchi themselves; it even acts on epinephrine-resistant preparations. Bronchodilatation is observed with doses of 1 μg. and over. The tidal volume increases by 10%. This bronchodilator effect was observed even on administration by inhalation (spray of 1% solution).

Many workers have independently stated that no histological lesions were ever observed in the tracheal mucosa of rabbits when 0.25% solution was used for inhalations, 10 minutes daily for 30 days. Konzett in 1940[16] showed that 1 mg./kg. body weight of N-isopropyl-noradrenaline, injected subcutaneously into guinea-pigs, relieved histamine poisoning and raised the minimal lethal dose considerably.

The toxicity of N-isopropyl-noradrenaline, given subcutaneously, was found by Dertinger, Beaver and Lands[17] to be 10 times less than that of adrenaline in white mice. The toxic dose in dogs is 10 times the therapeutic dose and in man is about 2,500 times the therapeutic dose, according to Cohen, Van Bergen and Knight.[18]

METHOD

No routine anæsthesia was used, the type of anæsthetic being always chosen according to the condition of the patient and to the requirements of the surgical procedure. Spinal and local anæsthesia were not included in these series.

Theophylline ethylenediamine was given in 0.48 g. doses intramuscularly as soon as the peritoneum was closed, and another similar dose was administered four hours after the operation, followed by 100 mg. orally 3 times a day for two days.

For N-isopropyl-noradrenaline a special mask was used (Fig. 1), designed by Dr. S. Linton. It incorporates a second part into which a plastic nebulizer makes a gas-tight fit, and which can be closed when not required. It would appear desirable to use a nebulizer giving as fine an aerosol as possible to reach the bronchial tree without being deposited on the nasal mucosa.

As soon as the patient had recovered sufficiently, he was given a nebulizer and instructed to inhale the aerosol 10 times every four hours.

From a practical point of view, the first of these two routines proved the easier to carry out, as many of the patients found the use of the nebulizer irksome in the immediate postoperative period, especially if they could breathe easily without it. On the other hand, patients with a tendency to bronchospasm were eager to use the spray for the relief it afforded.

RESULTS

The chief difficulty in an investigation of this nature is to ensure that the controls are really comparable cases. The patients were never selected, the routine being as follows: one was treated with theophylline ethylenediamine, one had no treatment, a third had N-isopropyl-noradrenaline and a fourth no treatment again, in sequence on the operation list.

TABLE II.

Agent used	*No. of cases*	*Incidence of cough*	*Percentage*
None	218	20	9.2
Theophylline ethylenediamine	100	6	6.0
N-isopropyl-noradrenaline	100	3	3.0

The χ^2 for theophylline ethylenediamine treated cases is 0.920 = P 0.35 (35%), which is not significant. The χ^2 for N-isopropyl-noradrenaline is 3.895 = P 0.04 (4%), which is very significant.[19] The results with the first drug are there-

fore likely to have arisen by chance, while the converse applies to the second. However much weight one gives to statistical evidence, clinical impressions cannot be ignored completely, especially when they apply to a reasonably large series of cases. Our finding is that both groups of treated cases showed markedly improved power of pulmonary ventilation over controls, and there has been no case of major respiratory complication amongst them, though the series is too small to place undue emphasis on this.

The dosage adopted was entirely empirical, and bigger or more frequent doses might be employed with advantage.

CONCLUSION

Our results prove statistically and clinically that by merely dilating the bronchi, postoperative chest complications can be significantly decreased. Therefore, we deduce that, other factors being equal, bronchoconstriction is the fundamental cause of postoperative cough. The bronchospasm in question is probably originated by a vagal reflex arising from peritoneal stimulation, which necessarily follows the surgical procedure. It cannot be denied that micro-organisms and anæsthetic agents may worsen the condition.

Sellick[20] had negative results with procaine-penicillin and breathing exercises. Scott *et al.* had good results with administration of carbon dioxide, but it must be kept in mind that CO_2 is also a bronchodilator.

This theory could perhaps only be proved by giving as much atropine (1/10 grain or 6 mg.) as is necessary to paralyze the vagus completely, but who would do this to a patient for the patient's own sake? We are rather inclined to think that a non-toxic bronchodilator that can be easily administered is the solution to the problem of postoperative chest complications.

SUMMARY

A series of cases were treated after operation with bronchodilator drugs. The use of theophylline ethylenediamine and N-isopropyl-noradrenaline led to a lower postoperative cough incidence than in an untreated control series, though the difference was statistically significant only in the case of the second drug. The clinical impression formed was sufficiently definite to justify a continuation of the trial.

We must express our thanks to the surgical and nursing staff of the West Suffolk General Hospital for their help and co-operation; to Dr. S. Linton of Lewis Laboratories Ltd., for the provision of apparatus and of N-isopropyl-noradrenaline; to Berger Laboratories Ltd., for help and advice.

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TRANQUILLIZING DRUGS

"The use of the tranquillizing drugs is resulting in an alarming tendency to institute immediate medicinal therapy for symptoms of psychogenic origin without giving any attention to the source of the presenting symptoms. The patient-doctor relationship is being impaired, and emotionally disturbed patients are being encouraged to turn to unprofitable defence mechanisms in dealing with their psychological problems.

"The immediate prescription of a tranquillizing drug for an emotionally disturbed patient, before an attempt has been made to tackle the disturbed psyche on a psychological basis, represents, in my opinion, a deplorable approach to clinical medicine. These tranquillizing drugs are contributing vigorously towards the elimination of the psychosomatic approach in modern medicine. If they were producing dramatic results there might be some excuse for their liberal use, but this is far from the case."—Letter to the Editor, *South African M. J.*, 30: 504, 1956.

Case Reports

GENERALIZED CYSTICERCOSIS WITH CEREBRAL INFESTATION*

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MICHAEL LENCZNER, M.D., *Toronto*

TÆNIA SOLIUM now rarely occurs in Canada, and in 1954 only four cases in pigs were reported from Western Canada by the Veterinary Director General.

Human cysticercosis presents therefore no problem, but with the influx of immigrants from South America, Mexico, Eastern and Southern Europe and India, the possibility of cases of human cysticercosis is to be borne in mind. The following case histories are an example of the above.

CASE 1.

Mrs. G.P., a 33-year-old Italian woman, came to Canada two years ago. She was born in a small village in Southern Italy in a poor agricultural district with very inadequate hygienic measures, where humans and animals intermingle freely, sharing to a great extent the already poor amenities of housing. She had scanty schooling and an unsettled family life. Married at 17, she had three children, now aged 9, 12 and 15 years. She was well, apart from minor childhood illness, an occasional brief febrile episode, until 1947. At that time she awoke one morning feeling ill, with general malaise, abdominal pain, tinnitus, vertigo and violent vomiting of large quantities of bile. She became restless, developed twitching movements of her limbs, became unable to speak and finally lost consciousness. She remained so for three days, with recurring vomiting and convulsions.

On recovery she had daily seizures of various types. She was investigated in two hospitals in Italy and was told she had gallbladder disease. Since then she has continued to have several types of seizures, the descriptions of which vary greatly. She usually has some warning, with blurring of vision and a feeling that something terrible is going to happen. She has definite grand mal seizures involving chiefly twitching of the left face, with mild jerking of the hands and feet, lasting about 10 minutes. About once every 10-14 days she has an attack of nausea and vomiting, with tinnitus and vertigo, followed by a more severe grand mal seizure with incontinence and unconsciousness which may last for a day or so. She also has attacks in which she complains of paralysis, starting at her feet and spreading up to involve her trunk and arms, with eventual loss of consciousness, lasting for 20-30 minutes. In other attacks she becomes "rigid all over" for about 10 minutes. She has been observed in attacks in which, while talking, she suddenly stares into space for a matter of a few minutes. Her husband states that at times when talking normally she suddenly goes to sleep and remains so for 2-3 hours. At other times, when laughing heartily, she suddenly becomes paralyzed and falls to the floor unconscious for a minute or so.

*From the Outpatient Department, Medical Clinic, Toronto General Hospital.

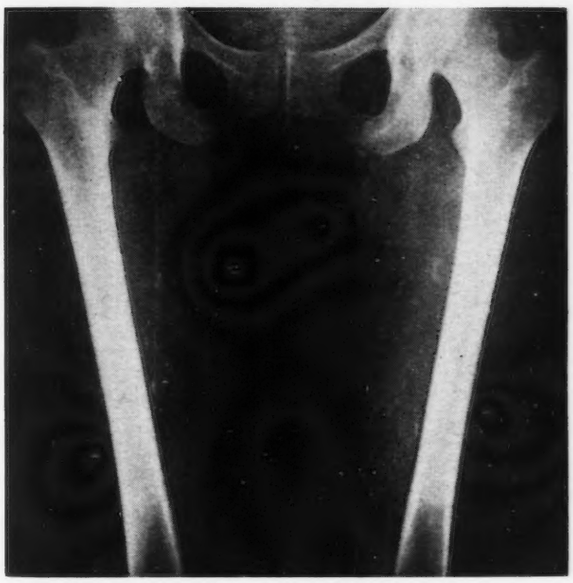

Fig. 1. Case 1. (G.P.).—The soft tissues are filled with numerous calcified densities, some bigger, some smaller, some linear, some in the form of capsules representing calcified larvæ of *Cysticercus cellulosæ*.

The physical examination of the patient in April 1955 did not reveal a great deal. She looked well and was well-nourished; the skin, subcutaneous tissues and muscles were everywhere normal. Head and neck were normal. The chest was within normal limits. The heart was normal—B.P. 120/74, pulse 72, regular. The abdomen was normally soft, no masses were encountered, the colon was contracted throughout and tender on pressure. The liver was palpable, the spleen not palpable. The joints and bones appeared normal. There was no impairment in the central nervous system. The fundi were normal. While the patient was undergoing examination, she had a petit mal seizure lasting approximately 5 minutes. The urine was normal. The blood count: red cell count 4,000,000, Hb 82%, white cell count 9,450 with 2% eosinophils, and 78 eosinophils per c.mm. on a direct count. The sedimentation rate was 14 mm. in one hour. Cephalin cholesterol flocculation and bromsulphalein retention tests were normal. Stools were negative for parasitic ova. The skull radiograph

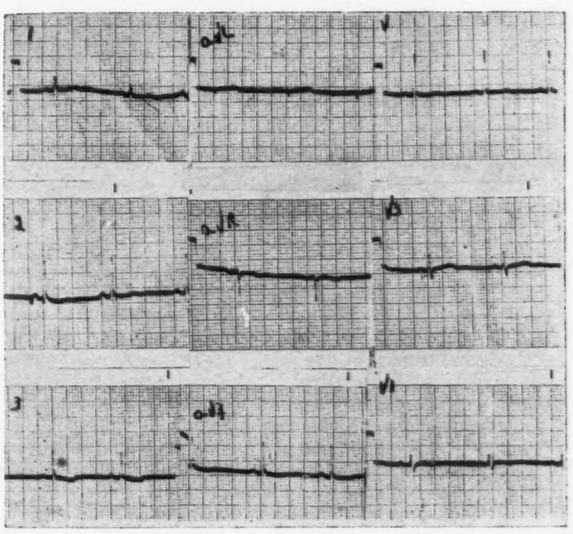

Fig. 2. Case 1. (G.P.)—The electrocardiogram appeared abnormal with flat or low negative T waves in almost all leads in keeping with diffuse myocardial damage.

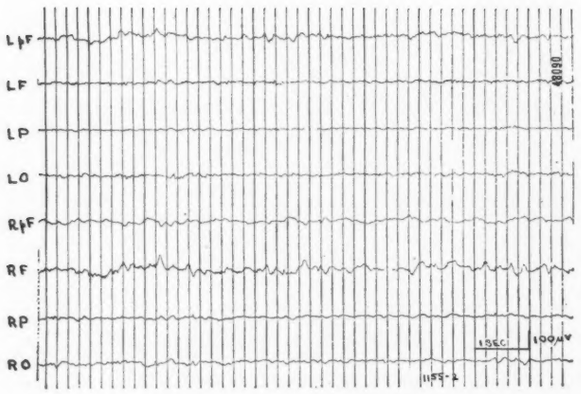

Fig. 3. Case 1.—The electroencephalogram showed a diffusely disorganized record with an abnormal focus in the right fronto-temporal region, with paroxysmal features suggesting epilepsy.

was normal, showing a well-calcified pineal gland without shift. Radiographs of the thighs (Fig. 1) showed the soft tissues to be filled with numerous calcified densities, some bigger, some smaller, some linear, some in the form of capsules representing calcified larvæ of *Cysticercus cellulosæ*. Other muscles, i.e. the glutei and the soft tissues of the abdomen and the recti, were filled with innumerable densities and calcifications of the same nature. The cholecystogram showed that the gallbladder filled and concentrated the dye, but possibly to a slightly decreased degree. The electrocardiogram (Fig. 2) appeared abnormal, with flat or low negative T waves in almost all leads, in keeping with diffuse myocardial damage. The electroencephalogram (Fig. 3) showed a diffusely disorganized record with an abnormal focus in the right fronto-temporal region, with paroxysmal features suggesting epilepsy in the record. The impression was of generalized cysticercosis with cerebral and myocardial infestation.

The patient was admitted for an air encephalogram on November 14, 1955. Lumbar puncture revealed normal spinal fluid pressure with negative Wassermann and colloidal gold tests, and a protein value of 23 mg. %. The air encephalogram (Fig. 4) showed asymmetry in the lateral ventricles, the right being larger than the left. The patient is being treated with Dilantin (diphenylhydantoin), Mysoline (pyrimidone) and barbiturates with considerable reduction of the paroxysms in intensity and frequency. Regular control visits are made.

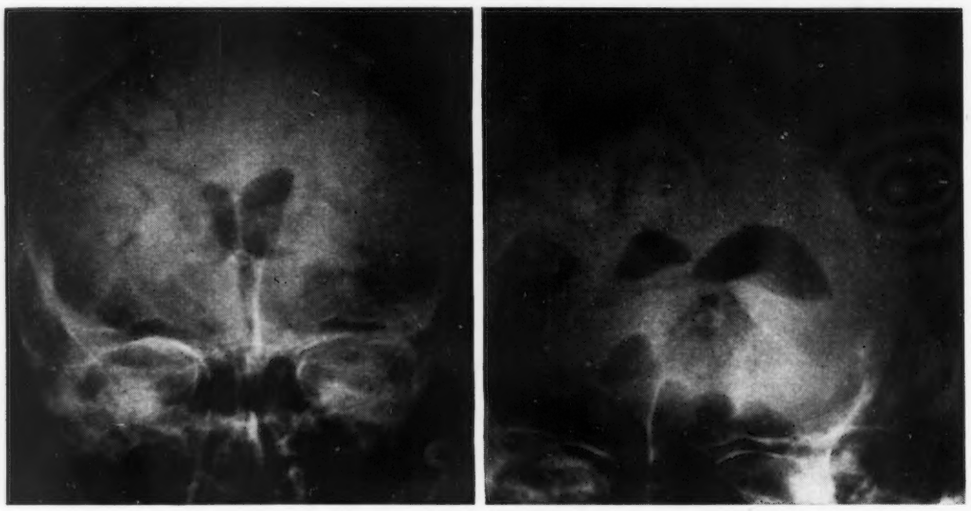

Fig. 4a Fig. 4b

Figs. 4a and 4b. Case 1. (G.P.).—The air encephalogram showed asymmetry in the lateral ventricles, the lateral right being larger than the left (2 views).

CASE 2.

Mr. J.S., 46 years old, was born in the Ukraine in a small village in a poor farming district with very rudimentary hygiene, where domestic animals and humans intermingled freely indoors and outdoors. During the First World War he lived for two years in a refugee camp in Russia in a barn shared by many women, children and domestic animals. In 1916-1918 he lived with his mother in an orphanage in Russia where he contracted typhus. He came to Canada in 1929. He was well until 1934, when he had a gastrointestinal hæmorrhage with black stools but no hæmatemesis and was treated conservatively in the Toronto General Hospital. In 1937 he was admitted to the Toronto General Hospital complaining of dizziness and loss of speech twice in four weeks and loss of comprehension of words for a few minutes, right-sided frontal headache for 3-4 days, fatigue and loss of weight, general weakness in arms and legs, more on the right side, and aching pain in the lumbar region. He was discharged with a final diagnosis of duodenal ulcer and petit mal. In November 1937, he came to the Medical Clinic with numbness and pain over the right eye, on one occasion associated with inability to speak. In 1939 he had two episodes in bed consisting of inarticulate noise, heavy breathing, stiffening of the body but no biting of tongue, no clonic convulsions or loss of sphincter control. These attacks have been described by family members. The attacks were followed by right frontal headaches, fatigue and inertia. He seemed to have had several of such attacks since his first gastrointestinal hæmorrhage. In 1939, a diagnosis was made in the Neurological Clinic, T.G.H., of epilepsy or cerebral spasm. In January 1942, he was treated again conservatively in the Toronto General Hospital for hæmorrhage and duodenal ulcer.

In December 1943, he was admitted to the Mayo Clinic, Rochester, Minnesota, for partial gastrectomy of posterior Polya type. A skull radiograph showed a small area of calcification in the meninges over the right frontal lobe and a contiguous meningioma was suspected. He was reasonably well until 1946 and worked as a truck driver, but at this time started to have frequent right-sided headaches, increasing fatigue, lack of energy and difficulty in remaining awake. He was seen to have another seizure while driving, with an

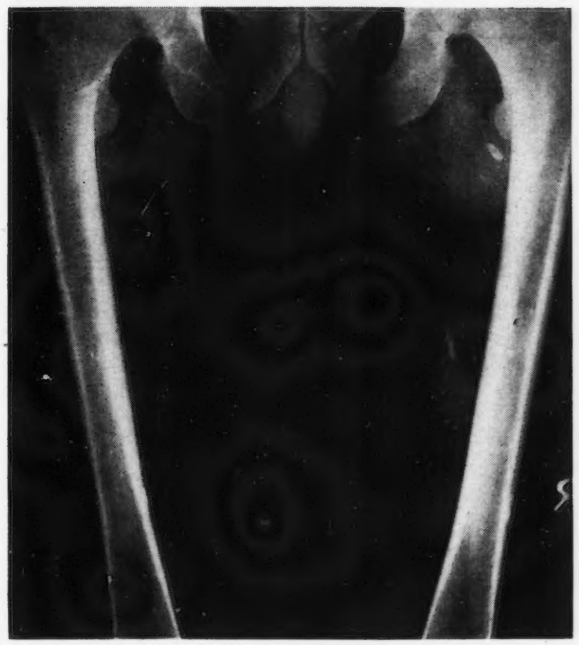

Fig. 5. Case 2. (J.S.).—Calcific densities in the soft tissues of the thighs, ranging in length from a few mm. to a couple of cm., representing calcified cysticerci.

outcry of inarticulate sounds, heavy breathing, foaming and convulsions followed by prolonged sleep and right frontal headache. He began to take amphetamine and Bromo-Seltzer and large quantities of APC tablets to combat his fatigue and headaches. In 1950 he was in Toronto East General Hospital with abdominal pain. At that time an appendectomy was performed and his old gastrectomy scar was opened, but nothing abnormal was found.

From 1951 till the present time he had no permanent form of employment. He worked at various jobs, but became very fatigued, unable to concentrate, very irritable and dismayed. When taking Bromo-Seltzer, Dexedrine (d-amphetamine) and APC he felt better for short periods. In September 1955, he was admitted to the Toronto Psychiatric Hospital, where he remained until November 1955, being discharged with a diagnosis of a drug addiction on the basis of inadequate personality. He was found to have sulfhæmoglobinæmia and anæmia (60% Hb), and was referred to the Toronto General Hospital for further investigations. These showed no abnormalities on physical examination except for a marked pallor of the skin and mucous membranes, with no stomatitis or glossitis.

The urine was normal. Hæmoglobin 7.5 g. %, red cell count 4.8 million, white cell count 9,200 with normal differential, hæmatocrit 32%. The blood smear revealed hypochromia but little microcytosis. The sedimentation rate was 21 mm. in one hour. Blood serology was negative. Serum calcium level was 8.9 and 8.7 mg. %. Serum phosphorus level was 2.8 mg. %. Alkaline phosphatase was 8.6 King-Armstrong units. Serum electrolytes were normal. The non-protein nitrogen was 30 mg. %. The stools were negative for occult blood, fat globules or meat fibres, ova, cysts or parasites. Fasting gastric analysis revealed a histamine-fast achlorhydria. A xylose tolerance test for gastrointestinal absorption was within normal limits. A barium enema showed no abnormalities. An upper G.I. series revealed rapid transit from the stomach to the small intestine; there was no evidence of stomal ulceration. A small bowel follow-through examination revealed a completely normal small bowel. Skull radiographs showed two small areas of calcification in the right frontal region compatible with an encysted larva of *Cysticercus*. In the lateral view a linear calcific density in a tongue of the parotid gland, representing a calcified cysticercus, was found. X-ray of the thighs showed the presence of multiple fusiform calcifications in the soft tissues ranging from several mm. to several cm. in length. An electroencephalogram was within normal limits. On repeating the latter two months later, epileptic paroxysms were seen during hyperventilation, and evidence of a localized abnormality near the occipital pole and in the right temporal region was obtained. The patient improved on oral iron therapy, proper diet and a small amount of barbiturate at night and is being followed up regularly.

Final Diagnosis: (1) Hypochromic anæmia after subtotal gastrectomy for duodenal ulcer; (2) generalized cysticercosis with cerebral calcification and personality pattern disturbance.

PATHOLOGICAL ANATOMY

If man ingests eggs of *Tænia solium* contained in human intestinal content or if mature proglottids are forced into the stomach by reverse peristalsis, the embryos are liberated by the action of gastric juice. The tapeworm larvæ, known as *Cysticercus cellulosæ*, invade the intestine, enter the blood and are distributed to all tissues of the body. Full development takes place in the subcutaneous tissue, brain, orbit, musculature, heart, liver, lungs and peritoneum, with the formation of a cyst. Each cyst consists of a clear, translucent membrane with an opaque white spot at one point, representing the worm. Microscopically a surrounding fibrous capsule is seen, infiltrated with eosinophils and polymorphonuclear leukocytes. After several months or years many of the worms die and there is a conspicuous reaction with necrosis of the worm and some of the surrounding tissue, infiltration with eosinophils and polymorphonuclear leukocytes, formation of giant cells and eventually calcification.

The cysts produce symptoms almost entirely because of the pressure on surrounding structures. Many instances of epilepsy are believed to be caused by cysticercosis of the brain.

Cysticercosis is found in all parts of the world where *Tænia solium* is found, but especially in those regions where personal hygiene is at a low level. Bruns[3] describes a symptom complex consisting of a sudden onset of violent headache, vomiting, tinnitus and vertigo, passing on in the more severe attacks to deep coma and even death, and often precipitated by sudden movements of the head. It was considered to be diagnostic of a solitary cysticercus in the fourth ventricle with acute intermittent obstructive

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hydrocephalus. The solitary intraventricular cysticercus is, however, not the only cause of acute obstructive hydrocephalus.

Bickerstaff *et al.*[6] describe a racemose form of cysticercosis, which is apt to form at the base of the brain and, being a mobile structure sometimes with a long pedicle, is capable of intermittent blocking of the roof foramina of the fourth ventricle. Disturbance of equilibrium and spasmodic ataxia may accompany attacks of obstructive hydrocephalus; more progressive disturbance of equilibrium without marked ataxia of the limbs when supine accompanies posterior fossa racemose cysticercosis, simulating a tumour of the vermis of the cerebellum.

Lesions in the ventricular system or in the posterior fossa, followed by long-standing raised intracranial pressure, may lead to impairment of vision and consecutive atrophy of the optic disc. Involuntary movements of different localization and grand mal seizures have been described as consequences of cerebral cysticercosis. Changes in personality in patients suffering from cerebral cysticercosis have been noted.

CONCLUSION

Two cases of generalized cysticercosis with cerebral infestation are reported in immigrants to Canada. In one, evidence of myocardial infestation was obtained; in the other a personality pattern disturbance was brought to light. The importance of an accurate personal history in regard to soil and seed of the infestation and the manifold symptoms is considered. The diagnostic value of radiography of the thighs, a selective site of calcific densities of cysticercosis, is pointed out. The need for awareness of the possibility of cerebral cysticercosis in immigrants from South America, Mexico, Eastern and Southern Europe and India is stressed.

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RESIDUAL PULMONARY COCCIDIOIDAL GRANULOMA*

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COCCIDIOIDOMYCOSIS is an acute or chronic pulmonary infection caused by the fungus *Coccidioides immitis*. It is endemic in parts of the southwestern United States and Central and South America. Most cases which occur elsewhere can be traced to residence or travel in the endemic regions, as in the case reported here, or to contact with materials from these regions, as in the Canadian case reported by McLetchie *et al.*[1]

That coccidioidomycosis may occur in an unapparent or asymptomatic form and leave residual pulmonary granulomata has recently become better appreciated.[2] However, in areas where coccidioidomycosis is not ordinarily encountered, the coccidioidal residual may be overlooked in the differential diagnosis of so-called "coin lesions". Attention to a history of residence or travel in endemic areas and application of the coccidioidin skin test may supply leads.

The etiological diagnosis of chronic granulomata in surgical specimens by routine histological techniques often presents considerable difficulty. Simple techniques for the identification of possible etiological agents are, therefore, of considerable interest. In the present case, the diagnostic spherules of *Coccidioides* were demonstrated in a pulmonary granuloma by a concentration method hitherto not applied for this purpose.

Mr. E.O., a 35-year-old farmer, was referred to the University of Alberta Hospital on June 19, 1955, because of a single discrete chest lesion discovered on a film taken by the mobile x-ray unit on April 18, 1955. His only complaint was of a productive morning cough which had been present for years and had not changed.

He had worked in Arizona from February 1951 to February 1952, and stated that "valley fever" was prevalent in this region. He could recall no fever or illness during this period.

His temperature and sedimentation rate were normal. His chest was clinically clear. Chest x-rays and tomograms confirmed the presence of a single discrete opacity about 2 cm. in diameter in the apical segment of the left lower lobe (Fig. 1). Sputum smears were negative

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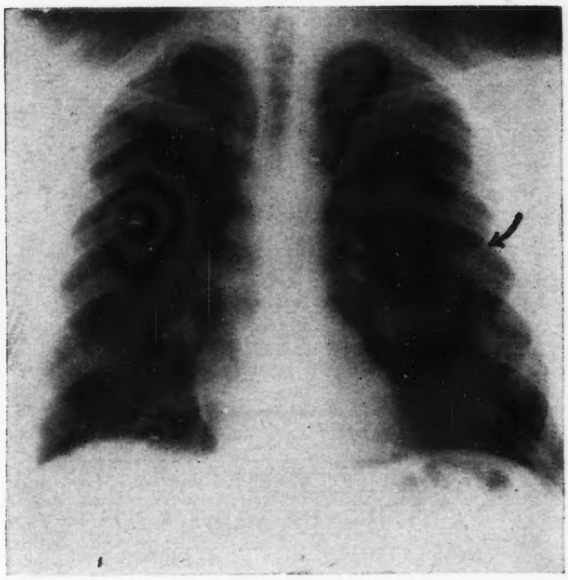

Fig. 1.—Discrete spherical opacity in apical segment of left lower lobe. Residual pulmonary coccidioidal granuloma.

for tumour cells and for tubercle bacilli. Sputum cultures grew a few *H. influenzæ*, but cultures were negative for *M. tuberculosis*. The hæmoglobin value was 16.5 g. per 100 c.c. The white cell count was 8,600 with a normal differential. The tuberculin skin test was negative to 1/20 and 1/10 mg. of old tuberculin. The coccidioidin skin test was positive.

Barium enema, barium examination of the stomach and duodenum, and sigmoidoscopic examination had been negative on investigation prior to his referral. Intravenous pyelograms showed poor filling on the left side, but retrograde pyelograms were normal. Bronchoscopic examination and bronchograms added no further information.

Thoracotomy was performed on June 27, 1955, and the lesion was removed by wedge excision.

LABORATORY DIAGNOSIS

The operative specimen consisted of a wedge of lung tissue 5 x 3 x 2 cm. Two surfaces and one margin were covered by thin, smooth, shiny pleural membrane. Bisection of the specimen revealed a discrete, raised, firm, grey nodule 1.5 cm. in diameter. The cut surface had an appearance of peripheral lamination with a central area of caseation necrosis.

Half of the specimen was placed in 10% formalin and the remainder was subjected to bacteriological examination for tubercle bacilli.

Histology.—Sections of the spherical lesion stained by hæmatoxylin and eosin and by the periodic acid–Schiff (PAS) method showed a necrotic centre surrounded by a narrow zone of fibrosis. Peripherally there was a narrow margin of lymphocytic infiltration including a few localized lymphoid nodules, some of which contained germinal centres. Adjacent pulmonary alveoli contained small collections of mononuclear macrophages filled with reddish-brown, granular pigment. Scattered about the lung tissue were small collections of fixed histiocytes filled with carbon pigment. The central portions of the nodule were eosinophilic and structureless, except for the ghost-like outlines of a few necrotic blood vessels.

Careful search of the necrotic tissue revealed a few ill-defined spherules, the size and morphology of which were suggestive of *Coccidioides immitis*. The best of these is shown in Fig. 2. Meticulous examination was required to locate the structures, and in the many sections examined none of the spherules seen contained structures suggestive of endosporulation.

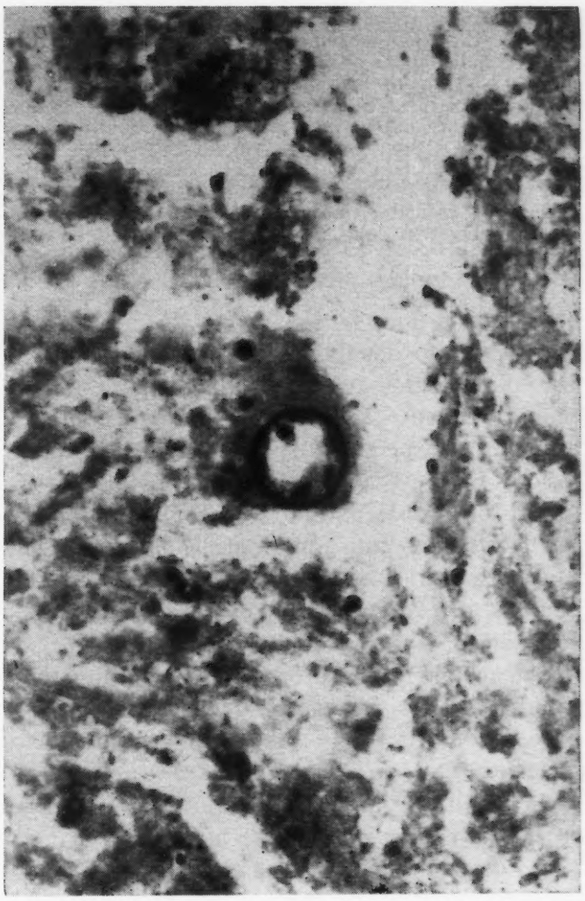

Fig. 2.—Spherule in necrotic central portion of granuloma; suggestive of *C. immitis* but shows no evidence of endosporulation. (H. and E. section. × 800.)

Bacteriological examination.—The portion of the specimen reserved for bacteriological study was ground up in a mortar, digested with approximately two volumes of 4% NaOH for 30 minutes at 37° C., neutralized with 8% HCl to pH 7 (Beckman pH meter) and centrifuged. Most of the supernatant fluid was discarded. Smears were prepared from the sediment and two Löwenstein slants were inoculated. No acid-fast organisms were seen in the smears, and there was no growth on the Löwenstein slants in eight weeks.

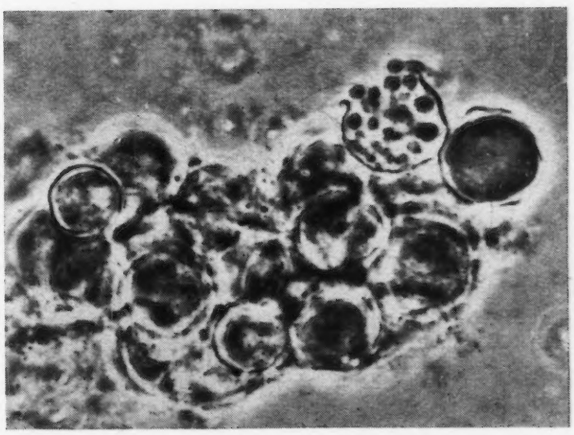

Fig. 3.—Group of spherules of *C. immitis* in sediment from alkali digestion procedure. Endosporulation is evident. (Lacto-fuchsin mount. Phase contrast. × 800.)

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Mycological examination.—A portion of the sediment from the digestion procedure was used for the inoculation of Sabouraud's, Littman's OSCV and blood agar media. No growth had occurred in three weeks. The remainder of the sediment was used in the preparation of wet mounts and permanent mounts in lacto-fuchsin.[3] These preparations revealed numerous spherules, some containing endospores diagnostic of *C. immitis* (Fig. 3). Whereas the few organisms seen in histological sections stained by H and E or by PAS techniques were considered suggestive, the mycological preparations were diagnostic.

COMMENT

Attempts to demonstrate etiological agents in chronic granulomata by examination of microscopic sections stained by various techniques are often unsuccessful, particularly in inactive lesions of long standing. The obvious desirability of supplementing such investigation by bacteriological and mycological cultural techniques requires no comment. The latter procedures may require from several days to weeks for definitive identification of the etiological organism. Therefore, procedures permitting more rapid diagnosis are of great value. In the case of *C. immitis,* use of the alkali digestion and concentration method described above may allow definitive diagnosis on the same day the specimen is received at the laboratory.

In the case of granuloma-evoking fungi other than *C. immitis,* the use of digested specimens would yield suggestive results only, since these organisms cannot be identified with certainty by their tissue phase alone. Further, none of the pathogenic fungi (with the possible exception of *Cryptococcus neoformans)* survives alkali digestion.[4] Therefore, a conscientious laboratory examination for the diagnosis of any chronic granuloma requires the routine inclusion of fungus cultures from fresh material as well as the usual pathological and bacteriological examinations.

SUMMARY

Residual pulmonary coccidioidal granuloma must be included in the differential diagnosis of so-called "coin lesions" in the chest, even in non-endemic regions. There may be no history of a related clinical illness.

The etiological diagnosis of chronic granulomata of long standing is often difficult, and in the case of *C. immitis,* demonstration of diagnostic spherules showing endosporulation may be difficult. By a simple alkali digestion and concentration technique large numbers of typical organisms can be demonstrated from lesions in which they are very difficult to identify by ordinary histological techniques.

We wish to thank Dr. J. K. Bigelow, Lethbridge, Alberta, who referred the case, and Dr. H. Meltzer, University of Alberta Hospital, who performed the operation, for the availability of the case material.

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INFECTION WITH PASTEURELLA MULTOCIDA FOLLOWING CAT BITE*

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IT HAS BEEN SHOWN in recent years that household pets, particularly cats, can be the source of somewhat unusual infections. A recently discovered disease entity, namely cat-scratch disease, first reported by Debré,[1] has overshadowed another infection frequently transmitted through the bite of a cat but not confined to this species of animal. This infection, with *Pasteurella multocida,* was first reported in the English literature in 1942 by Allin.[2]

Since this report in the literature about 60 cases altogether must have been recorded. Many cases, we are sure, have not been recognized because they were not examined bacteriologically or because many physicians are not aware of this type of infection. It seems, therefore, worth while to briefly report another case.

A 65-year-old woman was admitted to St. Joseph's Hospital after having been bitten by a cat in the right ankle five weeks before admission. The injured area had never healed and there was considerable inflammation in spite of treatment with penicillin, sulfonamides and aureomycin. The patient also used linseed poultices and hot foot-baths without success. On admission to hospital there was a fairly large swelling anteriorly over the right ankle with considerable erythema and a central opening through which pus drained freely. The abscess was surgically drained and at this time a culture was submitted to the laboratory. Organisms grown from this culture were Gram-negative bacilli which showed the cultural and biochemical characteristics of *Pasteurella multocida.* The organisms seemed highly sensitive to tetracycline, chlortetracycline, chloramphenicol and oxytetracycline, but were resistant to streptomycin and polymyxin. In spite of the surgical drainage the abscess

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failed to heal, and on April 22, 1955, the abscess cavity was again surgically drained, with removal of some small skin flaps and packing of the abscess cavity. Following this, another culture was taken which grew Gram-negative bacilli identical with the one cultured previously. In addition, a few staphylococci and diphtheroid organisms were found. However, in spite of the last procedure, the lesion on the leg failed to heal and a third surgical intervention had to be performed with débridement of the now ulcerated area and removal of skin edges and granulation tissue. A split thickness graft taken from the thigh was applied. The patient then made an uneventful recovery and was discharged from the hospital on May 28, 1955. While in hospital the patient received concurrently with surgical therapy quite extensive antibiotic medication with penicillin, streptomycin, and chloramphenicol, and later on also Achromycin and erythromycin. On the second isolation, however, the Gram-negative bacilli seemed to have shown considerable resistance to all antibiotics previously used, by the disc method. The Gram-negative organisms grown on blood agar showed abundant smooth growth, forming small round colonies aerobically, and also grew facultatively anaerobically. The organisms failed to grow on eosin-methylene blue agar. On smear the organisms were of bacillary form with pleomorphic appearance. An organism of the *Pasteurella* group was suspected and a culture was forwarded to the laboratory of the Department of Health of the Province of Ontario.

The biochemical reactions of this organism were: Nitrate—positive; Voges-Proskauer reaction—negative; methyl red—negative; indol—negative; gelatin—negative; bromcresol purple—mild, no change; H_2S—slight; dextrose—acid, no gas; xylose—acid, no gas; mannite—acid, no gas; saccharose—acid, no gas; sorbite—doubtful; lactose—negative.

On the strength of this, the organism was classified as resembling *Pasteurella multocida.*

REMARKS

The very recent literature shows reports of sporadic cases infected with this type of organism; Millar and Peterson[3] reported a case occurring in a trapper who injured his hand while working on the trapping line. Ewan[4] reported another case of meningitis due to the same organism occurring in a child who apparently was infected by a pet kitten from which *Pasteurella multocida* also had been isolated. More cases have been recently published by Neter,[5] and considerable work regarding susceptibility of this organism to different antibiotics has been done by the same worker. It is of particular interest that, generally speaking, *Pasteurella multocida* seems to be highly sensitive to penicillin and considerably less to streptomycin. Also generally speaking, the organism seems to be sensitive to chloramphenicol and the broad-spectrum antibiotics.

It appears, therefore, remarkable that this lesion failed to respond properly to what appeared to be adequate antibiotic therapy of organisms quite sensitive to the antibiotics as shown by the initial sensitivity test. One explanation of the unusual behaviour is that there was a very marked localized infection and abscess formation, into which the antibiotics failed to penetrate in adequate amounts.

SUMMARY

A case of abscess formation after a cat bite has been reported, from which *Pasteurella multocida* was isolated. The importance of bacteriological investigations of such lesions has been pointed out and the current literature has been briefly discussed.

The authors' thanks are expressed to Miss N. Cain, R.T., responsible for the technical work in connection with this case.

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CARCINOMA OF THE COLON AND ABDOMINAL WALL ABSCESS*

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ACUTE ABSCESSES of the abdominal wall are usually associated with lesions other than carcinoma, namely, some type of inflammatory process. In the past three years, however, three cases have presented themselves with abdominal abscesses as the first symptom and chief complaint. The underlying etiology in all three cases was colon carcinoma. It is the purpose of this paper to present these cases and to stress the fact that carcinoma of the colon must be kept in mind in the diagnosis of symptoms of this sort.

CASE 1

A 78-year-old white male was admitted to St. Paul's Hospital, Vancouver, in early November 1952, complaining of right upper abdominal pain, anæmia and weakness. Examination showed a tender mass in the right flank. There was leukocytosis, increased pulse rate and fever. Within four days the mass localized and began to point in the region between the right flank and right lumbar region. Incision and drainage were carried out, and 500 c.c. or more of yellow pus was obtained. Culture grew colon bacilli. There was fæcal drainage until resection later.

A barium enema two weeks later showed a lesion of the cæcum and ascending colon. Two weeks later the abdomen was opened and an extensive mass in the cæcum was resected by right hemicolectomy. A pathological diagnosis of "colloid adeno-carcinoma of the cæcum with metastases to the regional lymph nodes" was made.

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*Read before the B.C. Surgical Association at Harrison Hot Springs on April 22, 1955.

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The patient recovered sufficiently to be sent home. The abdominal incision healed but the flank incision continued to drain pus but no fæces, for the remainder of his life.

The patient died of generalized wasting and metastases in six months.

CASE 2

A 78-year-old white woman was admitted to St. Paul's Hospital in mid-June 1953, complaining of a large tender mass in the left upper quadrant. She had a leukocytosis of 18,000, fever and rapid pulse.

An abdominal wall abscess was diagnosed and incision and drainage carried out through a left subcostal incision; 700 c.c. of yellow pus was obtained. Colon bacilli and *Strep. fæcalis* were cultured. There was no fæcal drainage and the area healed uneventfully. Barium enema showed "diverticulosis in the distal transverse colon with some irregularity of the bowel in this area, possibly due to an inflammatory reaction".

The patient felt well for nine months, and then was readmitted to hospital after a mass could be palpated again in the left upper quadrant. Barium enema showed no essential change.

On April 8, 1954, the abdomen was opened through an upper transverse incision. An extensive carcinoma of the splenic flexure was found, involving the tail of the pancreas, the greater curvature of the stomach and the anterior abdominal wall. Another carcinoma was found in the cæcum. The liver was clear. The terminal ileum, entire colon to low sigmoid, tail of pancreas, portion of greater curvature of stomach, the involved mesenteries and omentum and a portion of abdominal wall were removed en bloc.

She made an uneventful recovery and died 11 months later of recurrence, including an ulcerating implant in the incision.

CASE 3

A 40-year-old white male was admitted to St. Paul's Hospital on April 24, 1954. He had been admitted to an out-of-town hospital six weeks previously with a left perinephritic abscess which was incised and drained. In a few days fæcal drainage began and continued.

After admission, barium enema showed almost complete obstruction of mid-descending colon. In spite of fæcal fistula drainage, obstructive signs developed and a transverse colostomy was necessary. This was done on May 5. On May 28, after a poor postoperative course, a left upper quadrant incision was made and 2,000 c.c. of thick yellow pus containing *B. coli* was drained from a left subphrenic abscess. He recovered rapidly and was sent home. On July 21, he was readmitted for barium enema. He had gained 40 lb. weight (from 80 to 120 lb.). Barium enema showed complete obstruction in the upper sigmoid, probably on a basis of diverticulitis.

He was readmitted in November and had a sigmoid resection for what appeared to be extensive diverticulitis. The wall in the left lumbar area and flank appeared involved in the extensive inflammatory process. An end-to-end anastomosis was done. The pathology report was "adenocarcinoma with metastases in the distal lymph nodes".

Recovery was uneventful. In January 1955, a repeat barium enema showed narrowing at the site of anastomosis. The tract continued to drain, but drainage was not fæcal. It was decided not to close the colostomy because of possible future obstruction.

The tract continued to drain, although the patient did well for a few months. He died in his local hospital in October 1955, of carcinomatosis.

Numerous articles have been written on perforation of the large bowel due to carcinoma, with peritonitis and intra-abdominal abscess, but only one article was found reporting cases in which an abscess of the abdominal wall had been the first sign of carcinoma of the colon. Lerch[1] reports three cases where an abdominal wall abscess localized in a position corresponding with that of the tumour and was the first symptom of the disease. He noted that this condition is usually a sign that the disease has reached an advanced stage, and that the prognosis is poor.

From the limited experience of our three cases we may make several observations:

1. Both right and left colon are involved in abscess formation.

2. It is difficult to differentiate between carcinoma and diverticulitis in carcinoma associated with abscess until pathological sections are made on the excised specimen.

3. In cases of colon carcinoma associated with fæcal fistula following abscess drainage, a persistent draining sinus develops after resection, or even after a defunctionalizing transverse colostomy, unless the involved abdominal wall is excised. This can be done with impunity on the anterior wall but in the lumbar or flank region, with extensive inflammatory reaction, it is doubtful whether chances of cure would be improved. Extensive excision with tantalum mesh repair may be considered. This was successfully used by Hull[2] in an extensive abdominal and thoracic wall resection for chondrosarcoma of the rib with extension into the colon.

4. One may conclude that abscess formation in the abdominal wall in connection with colon carcinoma makes for a uniformly bad prognosis. Although the abscess may be drained and the primary growth later resected, the malignancy has been disseminated by the abscess formation.

5. In each of these cases, although the abscess was responsible for the patient's seeking medical attention, the growth was very extensive and showed evidence of long standing.

6. In any case of abdominal wall abscess, carcinoma of the colon must be included in the differential diagnosis.

SUMMARY

Three cases of abdominal wall abscess associated with carcinoma of the colon are presented. Clinical observations are noted. The prognosis in cases of this sort is poor.

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Special Article

ORGANIZATION OF POSTGRADUATE MEDICAL COURSES

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[*The Postgraduate Medical Institute is a permanent, legally incorporated, non-profit, educational organization. It was organized in 1952 as a clearing-house for all information pertinent to postgraduate medical education in Massachusetts and New England. Its experience should be of considerable interest to those concerned with postgraduate education in Canada.* —ED.]

DOCTORS HAVE INDICATED their desire for continuing education, as demonstrated by the experience of the Postgraduate Medical Institute in Boston, Massachusetts. The Institute started its educational program as a natural outcome of the background informational services it had already developed. During its beginnings as a Survey of Postgraduate Medical Education, sponsored by the Massachusetts Medical Society in 1951, it had searched extensively through all the available records and sources, and prepared the most comprehensive physician list known in that area. At the same time, it had gathered information about existing course programs, assemblies, and other medical opportunities. It had brought information and doctors together through three publications: (1) YEAR ROUND: schedule of hospital activities: clinics, conferences, ward rounds, etc.; (2) COURSES FOR PHYSICIANS: list of regularly scheduled courses put on by the medical schools and other professional organizations; (3) WHAT GOES ON: a monthly bulletin of medical meetings and other special events, sent free of charge to over 19,000 doctors and hospitals under a contract with a well-known drug company. Through the past three years all of these lists have been expanded to cover the activities of the entire New England area. Functioning as a clearing-house, Postgraduate Medical Institute helps the societies, hospitals and various medical groups to dovetail their programs into an orderly timetable.

The Institute introduced its own pilot course in Boston in 1952, following which the physicians themselves requested that it inaugurate other courses in general medicine in more or less widely situated areas as a standard function. The purpose was not to compete with courses already in existence—that has been avoided without the slightest difficulty—but to reach the practitioner whose duties keep him somewhat confined to his own community. Today, courses are offered in nine different areas in Massachusetts and one in Rhode Island. The research, labor and expense entailed by the planning and operating of such programs has been justified by the enthusiastic response of the registrants.

PMI offers two types of course programs: (1) the hand-tailored program is built around subjects selected by a medical group in the area; if certain teachers are requested, every effort is made to engage them. (2) There is a long-term or package program (very popular in the areas), with a choice from four well-balanced courses. The most important and current aspects of general medicine are covered by this program in a four-year period. Each year, three or four subjects are intensively covered in 10 to 12 two-hour weekly sessions. The outlay to registrants is the same for both types of programs: a below-cost fee of $2.00 an hour. All courses are carefully devised by a Curriculum Committee, generally representing the schools of medicine and public health in Massachusetts, as well as subcommittees of experts in specialty fields. Suggestions of course registrants are always considered.

The members of PMI's Curriculum Committee appoint subject chairmen for the fields to be covered: allergy, arthritis, and related neuromuscular disturbances, cancer, cardiology, diabetes, endocrinology, gastroenterology, gynecology, hematology, hypertension and kidney disease, nervous and mental disorders, obstetrics, pediatrics, pulmonary disease, therapeutics, etc.

Course speakers are faculty members of medical schools and hospital staff members selected on the basis of their teaching and speaking ability. PMI keeps a confidential list of speakers wherein each is rated on these points. The list is also catalogued by subject, to guarantee prompt attention to requests for speakers.

PMI's constant research into all aspects of its service is demonstrated by the instruction given in area courses. Ideally, bedside teaching has been found most desirable, but impractical in many areas. Panel-type teaching has proved superior to the didactic lecture, since it grants latitude to both speaker and registrant; problems presented may be discussed at length; the spontaneous exchange of ideas sparks discussion and holds audience attention; the use of live patients, when indicated, is encouraged.

PMI considers an area eligible for courses on three conditions: (1) that it guarantees a minimum number (usually 25) of registrants; (2) that it agrees that the course will be open to all registered physicians regardless of affiliation; (3) that it establishes a committee of doctors representative of medical organizations and hospitals in the area and who, in turn, appoint a chairman.

The chairman then meets with PMI officials to discuss plans for his local group. He agrees to handle all local arrangements with the help of his committee. The meeting place must be in a convenient location and have adequate facili-

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ties and visual-aid equipment. The choice usually is a centrally situated hospital, approved by all, although the class is sometimes rotated among several hospitals, in order to satisfy all groups, or held in a neutral place such as a Soldiers' Home. As to time, Wednesday (the Massachusetts doctor's usual day off) seems to be preferred by most areas.

With the preliminaries attended to—minimum number of registrants guaranteed; all physicians in the area welcome; the day, hour and meeting place decided upon—the detail work begins.

The step-by-step procedure from this point on will be given, including mention of the specific letters, memoranda, check-lists, folders, etc., used, in their proper sequence. (A complete packet of this printed material is available to readers at a cost of $1.00.)

PMI sends the area chairman a memorandum in which he is asked to meet with his committee and select their program preferences, within two weeks if possible. A return postcard (listing the area's first, second, third, and fourth choice) is enclosed for their convenience. The memorandum contains an outline of the courses offered for the year, the number and titles of sessions, the chairman of each subject and the fees.

When the chairman's reply is received and committee's preferences are reconciled with those of other areas—as date of choice determines priority—the course program is then set up for each area. The speakers recommended by the subject chairmen are then contacted by telephone to participate in the various area courses. After this, a letter is sent with a return postcard for written confirmation.

Preliminary poster announcements of all PMI courses are sent to the area chairmen, medical schools and hospitals in Massachusetts, and adjacent hospitals in bordering states. These announcements tell in what areas the courses are to be held, along with the meeting place, time, day, and inclusive dates.

As soon as all speakers' engagements have been confirmed, the course program (a folder) is put in galley-proof form, proof-read, and printed. This folder contains all information about the program and a convenient enrollment coupon to be returned, with registration check, to PMI. Programs are mailed to every registered physician in the state, area hospitals, local medical societies, medical publications, medical schools, allied medical and scientific associations, and hospitals bordering Massachusetts.

Upon receipt of his registration and check, each registrant is then issued a book of numbered tickets by the Institute. Since admission to sessions is by ticket only, PMI is provided with an almost infallible means of determining attendance. This is important because all PMI courses are accredited by the American Academy of General Practice against the stipulated 150-hours-every-three-years requirement for membership.

Now a memorandum packet is sent to the area chairman. This includes a reminder, the details of which, if followed, will ensure efficient, comfortable meetings. The "Suggestions for Arranging Course Programs" memorandum itemizes such easily overlooked matters as hiring a reliable, experienced person to operate mechanical equipment (interns appreciate being offered this job), and having a capable course secretary to collect tickets, and receive telephone calls and messages for doctors attending the course, etc. This is a carefully prepared memorandum, the result of experience, which reduces to a minimum the chairman's possible margin of oversight.

Included in the packet is a list of equipment. The chairman is asked to check off whatever pieces are available—lantern slide projector, Kodachrome 2 x 2, Standard 3¼ x 4, movie sound projector 8 or 16 mm., blackboard, screen, etc.—and to return the list.

Also included is a detailed check-list for the course secretary, concerning such apparently trivial but vital details as having enough pencils, paper and ash trays on hand for each meeting, a pitcher of water and drinking glasses for speakers' table, and lights turned on.

A supply of mimeographed question forms goes to the area chairman for distribution among registrants at each meeting. These forms provide the audience with an opportunity to question the panel.

Comment forms—a mimeographed supply—are received by the area chairman. These, too, are for distribution at each session, and request the registrants to rate the session as excellent, good, fair, or poor, and to comment. The registrant may sign this form or not, as he chooses. Forms are analyzed and tabulated and speakers are appraised. The audience's collective opinion is of enormous value to PMI both immediately and in planning future courses.

Five weeks in advance of his engagement date, PMI sends to each speaker a memorandum concerning the procedures which, it assures him, will make for an effective session. Among other things, speakers are reminded to allow adequate periods for intermission—at least five minutes at the end of the first hour. The speaker is reminded to permit the other panel members enough time to note the written questions which have been submitted, and is asked to be sure to read each question aloud to the audience before discussion of it begins.

In addition to his meeting with the subject chairmen and all speakers, he is reminded that through preliminary discussion of their subject together, panel members will function more effectively, and the session, as a happy consequence, move forward with direction; often he will benefit from consulting with former

speakers and by visiting a session or two in advance of his own.

He is reminded of the value of preparing pertinent material (case histories, outlines, drug dosages, diets and exercise diagrams) for distribution amongst the registrants. PMI will mimeograph these for him and send them to him one week in advance of the meeting.

The incalculable value of audio-visual aids is impressed upon the speaker. One month in advance of his session, he is asked what equipment he will need and what material he will want mimeographed for the session.

If the speaker requests a live patient, the area chairman is so advised and in turn makes whatever necessary arrangements with the local hospital.

As the audience, in most cases, consists of general practitioners chiefly interested in diagnosis and treatments of practical value in office or home, the speaker is reminded to address himself principally to these categories.

Ten days in advance of his session, PMI mails to each speaker a travel sheet (a detailed map) showing highway route numbers, landmarks, the approximate mileage and driving time from Boston to course meeting. Train and plane information is also supplied.

PMI's other relevant duties, meanwhile, include keeping up to date a master schedule board of all courses being given in the areas; acting constantly as liaison between speakers, area chairmen and registrants; depositing course-fee checks, and paying speakers' fees and travel allowances. As previously noted, PMI keeps session attendance records for all areas, and, at the conclusion of each area's course, forwards course certificates to registrants.

PMI analyzes four different types of reports regarding each particular area's course program: (1) "Comments of Registrants"—the form distributed to audience at each session; (2) "Reports of Speakers"—mailed by PMI to each speaker after his particular session, together with an honorarium for his speaking engagement. He is asked to evaluate audience reaction, facilities, reception, etc.; (3) "Comments of Area Chairmen"—similar in content to the "Reports of Speakers" form; (4) "Ideas for Future Courses"—a questionnaire mailed, at the conclusion of the course, to all registrants.

In addition, PMI compiles for analysis various statistical data: number of doctors attending each course session, how many repeaters, how many new registrants, average distance travelled, members and non-members of the state medical society, etc. Further statistical studies on the correlation of subject matter are anticipated for the future, as are the cost components of the area education program generally.

Regarding costs, very little has been done nationally. The Postgraduate Medical Institute has tried to keep accurate accounting records since 1952. The difficulty in comparing ourselves with others involves the lack, as yet, of any nationally-agreed-upon system of measurement. Whereas PMI is totally responsible for every expense connected with its courses, other areas in the nation, as alluded to earlier, are more liberally endowed by universities, medical societies, or the state.

The position of the organization functioning in rent-free quarters, or with electricity supplied, or with personnel whose salaries are charged to some other appropriation, is very different from that of the organization that is responsible for every bill connected with a course, down to and including pencil sharpeners and scrap paper. This is by way of saying that speakers' fees of $200-$300 obviously cannot be considered the total cost of a course.

It is not feasible to include within this article the details of the cost accounting system which the Institute has devised over a period of three years in connection with the management of its courses. A separate article on this subject is in preparation.

It stands to reason that the main problem besetting the area courses is the expense of operating at a distance, which has the same effect on the central office as extended supply lines in military operations. However, service is the key word, since it encompasses all that the Institute represents, and it is hoped and anticipated that in the future this problem, like others in the past, will be satisfactorily resolved. Organizations such as PMI, which are offering education and information to the practising physician, are rendering a genuine service, whether directly or indirectly, to every citizen in the land.

If any of the foregoing information has proved helpful, or if we could further clarify any point, the reader should not hesitate to write us: The Postgraduate Medical Institute, 30 The Fenway, Boston 15, Massachusetts.

SUCCESSFUL RENAL ARTERIAL GRAFTS

What is thought to be a hitherto unrecognized syndrome of hypertension in adolescence is described by Poutasse and his colleagues from Cleveland (*J. A. M. A.*, 161: 419, 1956). They report three cases of severe hypertension in young patients, aged 14, 15 and 25 years respectively, apparently as a result of bilateral stenosis of the renal arteries. The stenosis was demonstrable by aortography. In the first two cases the outcome was fatal and at postmortem the artery was found to have a fibrous intimal proliferation, associated in one case with severe calcified atherosclerosis. When the third case appeared, it was diagnosed and treated by replacing the diseased portion of renal artery with a femoral artery homograft. Three months have elapsed since the second grafting and the patient remains in good health. This is thought to be the first successful arterial homograft operation on both renal arteries.

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ANOTHER ORAL DRUG FOR DIABETES

Judging by the excellent symposium published in the *Deutsche Medizinische Wochenschrift* for May 25 and June 1 (pages 823 *et seq.* and 887 *et seq.*), our German colleagues continue to maintain their lead in the field of investigation of sulfonamides with an antidiabetic effect. The present symposium is mainly concerned with an analogue of BZ-55 (*cf.* our June 15 number), in which an NH_2 group is replaced by a CH_3 group. This drug is known in Germany as D-860 and has as synonyms in Germany, Rastinon and Artosin, and in the United States, Orinase. Its main difference from BZ-55 is that it has no antibacterial action.

The German symposium contains work by clinicians, pharmacologists and other research workers from a number of German cities, including Freiburg, Frankfurt, Augsburg and Munich. Of main interest to clinicians is the first part of the symposium, in which a total of 781 cases studied in various clinics are discussed. The authors are particularly concerned with the criteria for assignment of cases to D-860 alone (*Einstellbarkeit*). They find many close similarities to the criteria for selection of patients for BZ-55 treatment. Thus, the older the patient the more likely he is to respond; 50% or more of patients over 40 years old were able to carry on on D-860. There was also a close correlation with the age at onset of the diabetes; 80% of persons whose diabetes had appeared after the age of 50 were able to use D-860 alone. There was a doubtful correlation with the length of the diabetes. The patients were divided into five constitutional types, and, as with BZ-55, the fat, sthenic type did best; whereas 75% of these persons were able to carry on on D-860 alone, only 20% of hyperthyroid types responded satisfactorily. The authors note that the response was not particularly marked in uncomplicated cases or cases with retinopathy alone, but was much better in cases with hypertension. They detected no deterioration in the cardiovascular system during treatment.

There was a negative correlation with insulin requirement; where over 40 units a day had been needed to balance the patient beforehand, the outlook for D-860 treatment was poor. The outlook for success with D-860 also diminished with increase in length of insulin treatment. One happy feature of D-860 was that hypoglycæmia rarely appeared, though mild subjective symptoms were noted in some ambulant patients. There was no effect of the drug on weight or the patient's mood. Side-effects appear to be less marked than with BZ-55, for in this series urticaria appeared only in seven cases, and jaundice in one. Constipation occasionally developed.

One effect which at first gave rise to unnecessary anxiety was the development of a precipitate in the acidified urine on addition of sulfosalicylic or picric acid. This was at first thought to be protein, but proved to be merely a harmless excretion product of D-860.

The general trend seems to be to start patients quite abruptly by discontinuing insulin and giving 3 g. D-860 a day, i.e., two tablets after each meal. The dose was then reduced, usually to one or a half tablet a day, within one to two weeks. As with BZ-55, raising the dose in resistant cases gave no positive effect; there was the same carry-over of effect after D-860 was discontinued, and this might continue for up to a few weeks. However, continuous use of the drug is advised. D-860 may be continued in mild infections, but for severe infections a little insulin should be added, and for surgery or pregnancy insulin alone should be used in diabetic management. In some cases a combination of D-860 plus insulin gave very good results. BZ-55 and D-860 appear to be quite interchangeable in therapy.

The effects of BZ-55 and D-860 on blood sugar and urinary sugar and in tolerance tests appear to be similar. D-860 causes a fall in total lipid and total cholesterol in the blood and has no effect on adrenocortical excretion or on the thyroid or the gonads. After six months it pro-

duced no demonstrable effect on the alpha-cells of the islets of Langerhans. Very careful study of blood and bone marrow revealed no toxic changes.

Animal experiments showed that D-860 was not stored in the organs; 90% of D-860 tagged with radioactive sulphur was excreted within three days in the urine. There were only two discrepancies between clinical and animal investigations. Firstly, the serum potassium level tended to fall in animals, while serum phosphate levels rose; this was not so in human subjects. Secondly, renal changes of a degenerative nature occurred with very large doses in animal experiments, whereas no signs of renal function disturbances appeared in diabetics.

To sum up, it would seem so far that D-860 in therapeutic doses is a well-tolerated and non-toxic substance. Like BZ-55, it is in no sense a cure for diabetes, and its future reputation will depend on intelligent selection of suitable cases. It is too early to say anything about its long-term usefulness in diabetes. Time alone will reveal this.

Editorial Comments

THE RELATION OF FOOD AND EXERCISE TO ATHEROSCLEROSIS AND CORONARY THROMBOSIS

We make no excuse for again mentioning these fascinating inter-relationships recently discussed in these columns.

As shown by Morris[15] for the United Kingdom (and applicable also to Canada), until about 1900 death rates in middle age were high for both sexes. Since then rates fell sharply until the 1920's. Then something happened. Female mortality continued downward, but reduction in adult male mortality slackened and almost stopped. Death rates for men, which were about 10% higher than for women a hundred years ago, and 33% higher after the First World War, are now 90% higher. The diseases involved are coronary thrombosis and cancer of the bronchus as major causes of death, and duodenal ulcer mainly as a cause of chronic sickness. It should be realized that there is now an epidemic of these conditions as lethal to middle-aged males as were tuberculosis, smallpox or typhoid fever in the past.

Sinclair's stimulating hypothesis[20] relates these conditions to a relative lack of essential fatty acids (E.F.A.), an excess of saturated fatty acids, and a low intake of vitamin B_6 or pyridoxine, due to our modern sophisticated diet. But obviously this is not the whole story. We must not forget the "host, agent and environment" concept, so eloquently stressed by John Gordon of Harvard, and stated somewhat differently as the idea of multiple causation of disease by Morris.[15] Conversely, these multiple causes can and must be isolated and identified.

We should clearly realize that atherosclerosis and coronary thrombosis are different, though related, conditions. Atherosclerosis is a condition from which even the late King Menephtah, traditionally regarded as the Pharaoh of the Exodus, suffered.[19]

As Barr[3] and others have pointed out, the development of atheromatous patches in blood vessels appears to be a specifically human disease. It is rare in other mammals. Furthermore, the term "atherosclerosis" should not be used indiscriminately to include anything from experimental fatty lesions in the aorta of rabbits to the whole of the natural history of ischæmic heart disease in man.[15] In this field, as in all others, we must avoid woolly thought.

As far as we can tell, the extent of lipid deposit differs little in men and women, but there is some precosity of its development in the coronary arteries of men. Atherosclerotic disease of the vessels of the legs is more common in men. Both men and women develop atherosclerosis with age, but there is evidence that the process is somewhat accelerated in males (Ackermann *et al.*,[1] White *et al.*[21]). There is historical evidence which suggests that coronary atheroma has *not* increased in recent years; but thrombosis and infarction have reached epidemic proportions. Only a minority of men with extensive coronary atheroma suffer infarction and, conversely, some with minimal atheroma may have serious obstruction and ischæmic heart disease.[13]

With this apparently contradictory evidence in mind, we will try to summarize the current situation in regard to lipids and the clotting mechanism.

Anfinsen[2] notes that lipids are transported in the plasma and through the extracellular fluids in three forms:

1. As chylomicra, which are large particles, usually visible under the microscope. They are mostly composed of triglycerides, but their detailed chemistry is at present unknown.

2. As beta-lipoproteins, which contain about 25% of protein and include varying proportions of cholesterol, triglycerides and phospholipids.

3. As alpha-lipoproteins, which contain relatively more protein and less lipid and so have a higher density.

As stated by Barr,[3] young women, in whom coronary thrombosis is rare, have lower cholesterol values than young men. Survivors of myocardial infarction have high cholesterol values, much of this in the form of beta-lipoprotein with an increase in S_f 10-20 bodies of Gofman.

Bronte-Stewart and co-workers[6] have made the reasonable assumption that any dietary

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factor which lowers the level of beta-lipoproteins will, by implication, lower the liability to myocardial infarction. These workers lowered beta-lipoprotein values in serum of volunteers by ingestion of olive oil, sunflower-seed oil, other plant oils and also seal and pilchard oil, i.e., oils containing unsaturated fatty acids. Animal fats or hydrogenated fats containing saturated fatty acids increased the beta-lipoproteins. Beveridge and co-workers[5] report a similar action from vegetable fats in their experiment.

Kuo and Joyner[11] have shown that anginal pain can be induced in patients with coronary atheroma after a fatty meal when lipæmia is maximal. H. W. Fullerton[9] has indicated that the coagulability of blood is increased after a fatty meal. Korn[10] has demonstrated that the clearing of fat from the blood after a fatty meal is brought about by a lipoprotein lipase which is a tissue enzyme. The enzyme is present in heart muscle and in adipose tissue. Its high degree of specificity of action on the triglycerides of the lipoproteins and chylomicra apparently depends on the presence of heparin, which may possibly be a component prosthetic group of this enzyme.[8] Robinson and Poole,[18] studying chylomicra in blood after a fatty meal, state that this increased coagulability is probably due to increased ethanolamine phosphatide, which is classified amongst the cephalins. Phosphatidylethanolamine is the classical cephalin composed of glycerol, two fatty acids in ester linkage, phosphoric acid and ethanolamine.[22]

Presumably then, in terms of Sinclair's hypothesis[20] in regard to saturated fatty acids, those ethanolamine phosphatides containing *saturated* fatty acids would produce clotting more readily than those containing *unsaturated* fatty acids. This opens up a great new field for biochemical research. What should be determined is whether the increased coagulability is due to an increased proportion of *any* ethanolamine phosphatides or whether it is due to a specific ethanolamine phosphatide modified by saturated fatty acids. Furthermore, to what extent is the whole physico-chemical clotting mechanism influenced by the increased proportion of beta-lipoproteins, as in survivors from myocardial infarction?

The physiological effect of exercise in regard to coronary thrombosis is of absorbing interest. It has been shown that men doing heavy work have half the rate of coronary disease of those doing light work.[14, 15] Mann and co-workers[12] have shown that normal males on a 6,000 calorie diet plus enough exercise to keep their body weight constant, failed to show significant changes in serum lipid constituents. When, however, the energy expenditure of the same males on the same diet was reduced to normal, permitting the consequent deposition of fat, there were significant rises in serum levels of cholesterol and phospholipids. This experiment was done on a small number of subjects, but the results are most interesting.

It would therefore appear that the middle-aged male, who is putting on weight, and who either does not take enough exercise to keep his weight constant, or eat less food to prevent weight gain, is courting disaster. If at the same time he gluts himself with animal fats, butter, cream and whole milk, he is precipitating a coronary episode. Hard physical work and frugality in eating still remain virtues in more ways than one.

So our tentative advice to paterfamilias is that he should eat less and keep moving. He should eat more plant and fish oils and less animal and hydrogenated fats. It seems that he should also eat more cellulose or roughage to promote the increased excretion of sterols via the stools as noted by Bersohn *et al.*[4] Mother already does much more physical work than her white-collar husband, and her female hormones in addition apparently protect her to some extent against coronary thrombosis.[3]

In South Africa, the death rate from coronary heart disease is higher in white females on a high fat diet than in Bantu (Negro) males on a low fat diet.[17] So that, materfamilias should not rely overly on the protection of her hormones. She should also eat moderately and avoid those cream cakes and pork chops.

When considering weight reduction, Connell[7] has provided a wise word of warning: "Weight reduction should be gradual!" He notes that overstrenuous weight reduction in an adipose arteriosclerotic patient too often appears to coincide with an episode of coronary or cerebral thrombosis. This is reasonable when one considers that too severe a drop in caloric intake actually places the patient on a diet higher in fats derived from his own fat depots.

HARDING LERICHE

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CYTOLOGY IN DETECTION OF CANCER OF THE CERVIX UTERI

The Johns Hopkins Hospital, Baltimore, formed a cancer detection clinic in 1947. Findings from this clinic are to be found in a recent article, "Role of Cytology in Detection of Carcinoma of Cervix", by Nesbitt and Brack (*J. A. M. A.*, 161: 183, 1956).

It is conceded by Nesbitt and Brack that biopsy is preferable for diagnosis of the early or late easily recognized gross lesion, just as dilatation and curettage is the only accurate method of diagnosis of cancer of the corpus uteri. This study also confirms the general belief that the smear is of value in the unsuspected case of early cancer. Of course, the study includes diagnosis of intraepithelial carcinoma of cervix, which seems to be diagnosed as frequently as the invasive disease.

A further benefit of cytology as a routine in the study of the clinically benign cervix lies in the more frequent diagnosis of basal cell hyperactivity, causing more interest in the follow-up of such lesions. Routine cytology also provides an opportunity for repeated observation of the non-invasive and suspicious lesions associated with pregnancy and infection (such as *Trichomonas vaginalis* vaginitis).

Statistics in the paper confirm the fact that positive and suspicious cytological findings must be followed up by biopsy if error is to be avoided. In 5,617 women examined, the incidence of malignancy was 3.8%. The initial smears were positive or suspicious in 86.1% of the malignant cases. The accuracy of the initial biopsies was 95.8%. Of the women with suspicious smears, 20.5% showed basal cell hyperactivity in the biopsy specimen, which provides a group of women for very valuable follow-up studies.

Unfortunately, the authors fail to state the number of clinically unsuspected cases in their "malignant" group, for these are the only ones which justify the added expense of cytology. In all fairness to the smear method, the cost of a cancer detection clinic cannot be compared solely with the number of unsuspected invasive lesions. The detection of non-invasive lesions has value, regardless of lack of uniformity in diagnosis and management. Only by the follow-up of such lesions will we ever be able to confirm or refute our present radical opinions on this subject.

The cost of this study is not stated. It is not of major importance, for it depends upon the local views of diagnostic criteria, techniques and standards. Detection clinics usually quote from $500 to $2,000 per diagnosed malignancy. At the usual estimate of $1.00 per smear or $2.00 per patient, the Johns Hopkins rate would be approximately $50 per diagnosed malignancy. This confirms the statement of Anderson and coworkers, who "very much doubt if the use of cervical smears as a routine gynæcological outpatient procedure would be justified, were they not convinced of the significance of the preinvasive or latent lesion." Others of us, who have more conservative views on the significance of carcinoma-in-situ and basal cell hyperactivity, would agree that the cost of cytology screening is justified if we are willing to investigate rather than increase the rate of immediate hysterectomy.

CRAWFORD B. SHIER

ACCIDENTAL POISONING IN CHILDHOOD

In a recent series of articles on accidental poisoning in childhood a careful appraisal was made of these frequently tragic and entirely preventable accidents. In Australia, where the surveys were made, statistics show that the death rate from such poisoning in children is not only higher than those in the U.S.A. and the U.K., but is still rising and it is therefore with a sense of urgency that the authors have set out to investigate causes and suggest methods of prevention. Conditions of life in the Dominion of Australia bear many similarities to those in Canada, in that large numbers of families live on farms and in country districts without electricity. Kerosene, insecticides and weed-killers are common household articles in both countries, and the Australian surveys show that of all poisons swallowed by children kerosene is the most common and the most accessible. Although no children in the authors' series died as a result of ingesting kerosene, almost half of them developed severe pneumonia. Weed-killers and pesticides on the other hand, although swallowed less frequently, accounted for a significant proportion of the serious and fatal cases. Only about 15% of the poisoned children had taken pills or other medication, but the highest case mortality was in this group.

What sort of children take poisons? Contrary to popular belief, these are not the mentally dull or neglected offspring of slatternly parents; they are unusually alert, inquisitive and experimental children, generally between one and three years old, and of fairly intelligent parentage. Nevertheless the poisons were frequently left within easy reach of these toddlers. Occasionally this was through failure to recognize the potentialities either of the substance or of the child, but in 60% of cases the substances were normally kept in a safe place and on the fatal occasion were actually in use or had recently been used and not returned to their proper place. This easy availability of the poison was found to be a factor of major importance in the causation of the accidents.

It follows that the question of prevention is really one of specific education of the parents.

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The poisonous nature of such common medications as seasickness cures, antihistaminics and ferrous sulphate is not generally appreciated by mothers, and the sugar coating often present on these tablets makes them particularly dangerous because they are not immediately spat out, as are the bitter-tasting purgatives and salicylates. Specific labelling, such as "Harmful to children—keep out of reach", could prevent many of the accidents that occur, and this would apply also to household articles like liquid furniture polish and patent carpet cleaners for example, some of which are in fact misleadingly labelled as "safety" products because they are perhaps non-inflammable. They may however contain chemicals which are strongly toxic if ingested. The present generation of parents is easily accessible through the media of press, radio and TV; in Great Britain, for instance, similar information is painlessly put across in such radio features as "Mrs. Dale's Diary". Every morning at coffee time the enormous majority of British housewives listen to a personal account of the daily doings of a typical British housewife. So deep is their sense of personal involvement that should one of Mrs. Dale's grandchildren, say, accidentally swallow her seasickness cure and be rushed off to hospital, while the listeners are kept in suspense until the next instalment, the lesson would be as deeply ingrained in the minds of British mothers as if their neighbour's child had suffered a similar accident. Could not the recently acquired addition to Canadian radio, the Plouffe family, be utilized in the same way for the good of Canadian children?

Here then is a public health problem, the solving of which is quite straightforward. It requires only energy and purpose on the part of the appropriate authorities to save many potentially valuable young lives and avoid an untold amount of grief.

ROSEMARY LINDAN

THE CONFUSION ENGENDERED BY FALSE PHILOSOPHIES

Often in our day-to-day reading we find ourselves with a vague feeling of disquiet. There are so many persuasive advocates of various systems of thought who experiment, then write to support their theses. In hunting through journals and texts for the solution to a patient's problem, we come across so much that is almost right, or not quite wrong, and we wonder in the confusion of our hurry how we can sort out the right from the wrong. How, in the permanent state of emergency in which we live, can we sort out the facts from the false philosophies?

If examined in detail, many of the parts of a false philosophy or theory seem rational or almost right or partly true. Unless examined critically, such fragments of truth give a false appearance of rightness to the spurious whole. This is true of almost all systems or "isms" based on the synthetic philosophical method of weaving whole cloth out of a few shreds of truth.

If one accepts a false theory or philosophy on faith, then two things go wrong. Firstly, the almost true doctrine may be accepted as true. Secondly, as we well know, the "righteous" have no monopoly of the right. The original error of judgment in accepting a wrong idea does not preclude accurate observation thereafter. If the observer then manages to rationalize or graft his findings even crudely on to his wrong philosophy, he will inadvertently be providing hardwood veneer for cheap furniture.

It is necessary to go back to the beginning—to the basic philosophical error from which the false system was synthesized. The system should be dissected by the scientific method so that its fallacy can be proven. Usually such an error was produced by a brilliant mind before there was sufficient scientific evidence to prove or disprove his idea. As the idea develops into an ideology and becomes veneered with truth, it is hard to find the chinks in the veneer. But by the time the average thinker becomes disturbed by the "almost rightness" of the basic premise, some scientific data will have accumulated to permit re-weighing the original evidence. This re-weighing should be done with careful attention to the possibility of introducing artefacts in the logical process of scientific dissection by the emotional ties due to the intimate association of the philosophy with one's own past.

Having dismantled the false synthesis, one can use rationally the individually true observations produced by some of its advocates. If these observations fit precisely with your philosophy, theory, or deductions, then well and good; make them an integer of a new grouping of ideas. If they don't fit accurately, your philosophy is in error, or the observations are in error, or the attempt to make them fit was in error. You may be trying to fit a Canadian moose into a Scottish landscape. An example is that contentious doctrine psychoanalysis which: (1) Involves acceptance of Freudian psychodynamics. (2) Involves acceptance of the principle that: (a) Pathogenic impacts on the human mind are carefully systematized and then consigned to a storage bin (or jail) where they continue to plague the person. (b) By bringing these jailed pathogens to the fore, dissecting them, and leaving them in the open, the patient will be healthy, having got rid of a "neurotic mechanism".

Some cannot accept (1) or (2) (a). Some can accept (b) by modifying it: "By helping some patients understand their own problem, they are better equipped to handle the problem themselves." The almost rightness of (b) often leads the unwary into thinking the whole doctrine is correct, which may not be true.

L. F. KOYL

Medical News in brief

RECTUM LIPOID GRANULOMA

Wittoesch and his colleagues from the Mayo Clinic draw attention once more to a distressing sequel of injection of oily solutions into hæmorrhoids. In a fair proportion of cases after a lapse of perhaps many years a granuloma may form in the rectum and give rise to vague symptoms, such as a feeling of fullness or constipation. The great danger is that the granuloma will be mistaken on clinical examination for a carcinoma and the patient submitted to an unnecessarily mutilating operation. The present authors examined records of rectal granuloma seen at the Mayo Clinic between 1941 and 1954 and found 23 lesions which proved to be lipoid granulomas (oleomas). Twelve of these patients gave a history of previous injection therapy for hæmorrhoids six months to 20 years previously. Diagnosis depends largely on the history and the results of biopsy. Treatment consists of local excision. It is pointed out that in oleoma the overlying mucosa is usually intact, though it may be ulcerated at a later stage.—*Proc. Staff Meet., Mayo Clin.*, 31: 265, 1956.

ŒSOPHAGEAL WALL GRAFTING

In Marseille, France, studies have been made of the use of serous membranes for reconstituting the œsophageal wall in dogs. Pleura and pericardium were used for this purpose in repairing large losses of substance of the œsophageal wall; there were 24% of postoperative deaths, 63% of survivals and 13% of cases of fistula formation. It is considered that pericardium is of great value as a plastic substance for this purpose and that it may freely be used after preservation in the cold.—Henry *et al.: Presse méd.*, 64: 952, 1956.

FETAL ANOXIA AND C.N.S. DAMAGE

Two French research workers, Minkowski and Sainte-Anne-Dargassies *(Rev. franç. études clin. et biol.*, 1: 531, 1956) have studied the relationship between fetal anoxia and damage to the central nervous system. They measured the oxygen saturation of fetal arterial blood at birth and examined the nervous system of the newborn, completing their investigations by taking an electroencephalogram and, in cases of fetal death, by histological examination of the lungs and the cerebral hemispheres. Their studies show a close relationship between anoxia and a pathological change in neurological signs at birth. They stress the importance of neurological examination at birth, conducted very exactly and repeated; this is of more importance than a study of respiratory symptoms or the EEG or general examination, in evaluating the infant's condition. They also mention that postmaturity may lead to fetal anoxia and therefore urge in certain such cases the induction of labour or Cæsarean section.

NYSTAGMUS IN ALCOHOLIC INTOXICATION

Howells of London, England, *(Brit. M.J.*, 1: 1405, 1956) draws attention to the value of the finding of nystagmus in motorists suspected of being under the influence of drink. In a series of volunteers given alcoholic drinks, nystagmus was the first physical sign to be noted in the eye and was always accompanied by an increase in reaction time. Its appearance suggests that a subject of average weight has received a minimum of 50 c.c. of absolute alcohol or its equivalent.

AMYOTONIA CONGENITA

The limp, floppy baby with muscle weakness and hypotonia presents a problem in diagnosis which can only be cleared up with time. The so-called syndrome of amyotonia congenita should be discarded, unless it is taken to mean the clinical syndrome of infantile hypotonia without any implications as regards prognosis. This is the conclusion drawn by Walton after a follow-up study of 109 cases which had been diagnosed as amyotonia congenita, usually in infancy, two to 25 years previously *(Lancet*, 1: 1023, 1956). In 67 of these children the disease had been progressive and 55 had died before the age of 12; twelve survivors were severely disabled. On the other hand, of the remaining 42 patients, eight had recovered completely and nine were only moderately disabled. In the remaining cases it had become clear that the diagnosis was incorrect; five patients had some form of muscle disease, six had a form of cerebral palsy and eight were mentally defective.

GASTRECTOMY FOR PEPTIC ULCER IN THE AGED

Davey and O'Donnell *(Lancet*, 1: 1033, 1956) make a plea for partial gastrectomy in the treatment of peptic ulceration in patients over 70. They base their belief that it is a reliable and rational treatment in the elderly on their experience in 30 consecutive cases of partial gastrectomy without mortality.

PREDNISONE IN TREAMENT OF CARDIAC ŒDEMA

Certain case studies have shown that prednisone (delta-l-cortisone) might act as a prophylactic against fluid retention and might even have therapeutic value in diminishing existing cardiac œdema. Riemer of the University of Colorado School of Medicine *(Bull. Johns Hopkins Hosp.*, 98: 445, 1956) has treated a patient with cardiac œdema completely refractory to other means by giving 2.5 mg. of prednisone three times a day. There was an immediate improvement in urine output, with rapid loss of œdema and restoration of cardiac compensation. It is suggested that further observations on this form of therapy be made.

(Continued on advertising page 40)

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REVIEW ARTICLE

ŒSOPHAGEAL HIATUS HERNIA*

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IN RECENT YEARS much has been written on the subject of œsophageal hiatus hernia, especially by thoracic surgeons, and gradually the idea has taken hold that this is a thoracic surgical condition and that the repair of this hernia is of necessity a trans-thoracic procedure. This is not necessarily true. Hiatus hernia should be very much the concern of the general surgeon and, in particular, of the abdominal surgeon. Just as with inguinal hernia, in which there are many methods of repair, some of which are specially adapted for certain anatomical and pathological states, so with hiatus hernia there are several methods of repair, some of which may be more suitable for one set of circumstances while others are more suitable for another.

Back in 1929 and again in 1937, Ogilvie[1] enunciated certain basic principles in inguinal hernia repair. In general, methods of repair which are at variance with these principles are unsound. This statement might equally well be applied to hiatus hernia. In both types of hernia there is a definite recurrence rate. This will probably always be so, and no infallible method will be found. But those methods which adhere most closely to the correct principles will be the most successful. In 1951 Allison,[2] in a classic article, outlined many of these principles and also clarified the types of hernia and their symptomatology. However, he did not, at that time, elaborate on the anatomy of the hiatus, and it is essential to consider the normal anatomy of this region in order to understand these principles.

ANATOMY

In this department numerous cadavers have been studied both in the autopsy room and in the dissecting room of the Department of Anatomy. The commonest arrangement has been found as follows (Fig. 1): The lower œsophagus passes through the posterior muscular portion of the diaphragm and is completely surrounded by the crura of the diaphragm. These crura split to form a muscular sling. The split occurs mainly in the right crus, but the left crus also contributes a small slip. The right border is made up mainly of the right crus, but also receives a small superficial slip from the left crus. This slip of the left crus arises from the median arcuate ligament which arches over the aorta above the origin of the cœliac axis artery. The left border is made up of the left crus, heavily reinforced by a large slip from the right crus, especially that portion of the right crus which arises from the median arcuate ligament. This large contribution from the right crus passes upwards and laterally, blending with the more vertically disposed fibres of the left crus on their anterior aspect. These arching fibres then pass upwards and anteriorly and decussate in front of the œsophagus separating that organ from the tendinous portion of the diaphragm (Fig. 2). Therefore, when the diaphragm contracts and descends, the splitting crural muscle draws the œsophagus downwards, increasing its angulation, and at the same time compresses it laterally, thereby producing a pinchcock action. Thus the right crus is the main guardian muscle of the hiatus. This is the explanation of the fact that a left phrenic nerve section may be used in treat-

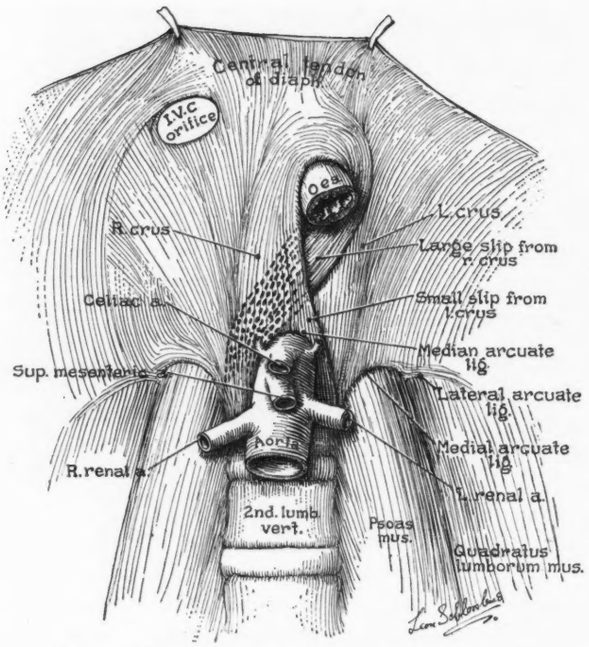

Fig. 1.—Normal anatomy of œsophageal hiatus.

THE ŒSOPHAGEAL HIATUS

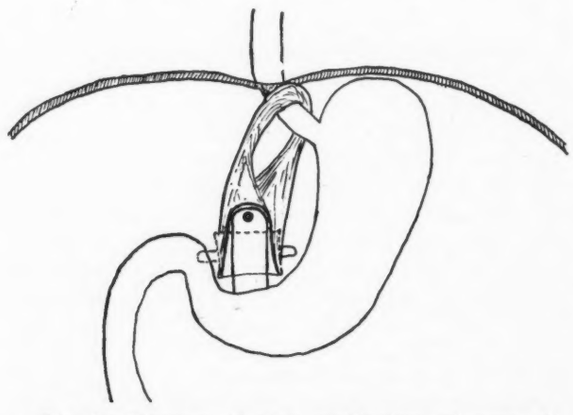

Fig. 2.—Diagram of sling mechanism of crura of diaphragm.

*From the Department of Surgery, University of Saskatchewan, Saskatoon.

ing some sliding hiatus herniæ. The action of the right crus is thus maintained and the sling-pinchcock action is maintained, while the left leaf of the diaphragm is paralyzed, letting the contents of the left subdiaphragmatic space rise up into the thoracic cage, whereby the œsophageal angulation from hiatus to cardia is increased. Collis, Kelly and Wiley[4] have, however, contested this theory, although they support the pinchcock action of the crura.

In some cases of hiatus hernia, those portions of the right and left crura which arise from the median arcuate ligament straddling the aortic opening may be deficient or degenerate, so that an unduly large lax œsophageal hiatus is produced. The decussation commencing posterior to the œsophagus is thus deficient (Fig. 3).

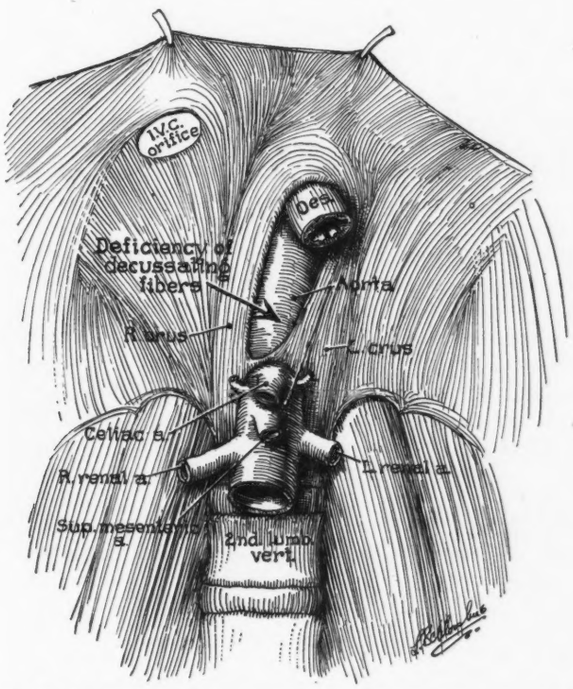

Fig. 3.—Pathological anatomy found in some cases of hiatus hernia.

The œsophagus is normally fixed to the margins of the hiatus by two structures. The first is the peritoneum, which is reflected off the anterior and lateral aspects of the œsophagus on to the under-surface of the diaphragm. This with its underlying fascia has more strength than is generally realized, but it can be stretched to form a false sac in a hiatus hernia. The second is the condensation of the fascia propria of the œsophagus which fuses with the subperitoneal fascia and blends with the fascial coverings of the upper and under-surfaces of the diaphragm. This tissue constitutes the so-called œsophagophrenic ligaments through which pass blood vessels to the œsophagus and in which are the vagus nerves. In hiatus hernia these ligaments are of necessity grossly stretched or deficient.

The normal hiatus will admit one to two fingers alongside the œsophagus, and the œsophagus can be invaginated into the chest a short distance but this distance is limited by the peritoneum and the œsophago-phrenic ligaments.

MECHANISM

The posterior mediastinal pressure is negative and the intra-abdominal pressure is positive. In straining and during muscular effort this latter pressure may be considerable. Therefore, from a functional viewpoint, gastric contents would naturally tend to regurgitate into the œsophagus. Most authorities agree that there is no functional muscular sphincter in the cardia. The competence of the cardia is therefore maintained by extrinsic factors. These are: (1) The acute obliquity of the entrance of the œsophagus to the stomach at the cardia, medial to the fundus. (2) The sling and pinchcock action of the crura surrounding the œsophageal hiatus. This tends to pull the œsophagus down and render it slit-like on diaphragmatic contraction, such as occurs in the Valsalva manœuvre, or on coughing, when the intra-abdominal pressure is raised. This fact is readily observed during œsophagoscopy performed under local anæsthesia. (3) The gas bubble of the stomach. This has not been stressed in the past, but it is hard to imagine that this peculiar arrangement of the fundus does not have a physiological basis. It is suggestive of the ball-valve float of the modern toilet tank, shutting off the inflow water when the tank is full. Rise of pressure in the stomach will increase the distension of the fundus so that the angle at which the œsophagus meets the stomach is rendered more acute.

This mechanism is probably the most important, as has been shown by Marchand,[3] and provides the most adequate explanation for all the various conditions in which regurgitation occurs or fails to occur. Thus in sliding hiatus hernia the œsophago-gastric angle is completely lost, so that free regurgitation occurs. In contrast, in a para-œsophageal hiatus hernia the œsophago-gastric angle is maintained and regurgitation does not occur. Also, in a combined type of hernia, i.e. a sliding plus para-œsophageal hernia, in which cardia and fundus move up together and maintain the same relative position to each other, regurgitation is again absent. The relief of symptoms in sliding hiatus hernia by a left phrenic nerve interruption is probably due to the eventration of the left leaf of the diaphragm, thereby letting the fundus expand further upwards and so increase the œsophago-gastric junction angle.

ETIOLOGY

The etiology of hiatus hernia is not clear. Some are undoubtedly congenital, for they are found in babies under three months of age, as has been pointed out by Belsey and Corner. This condi-

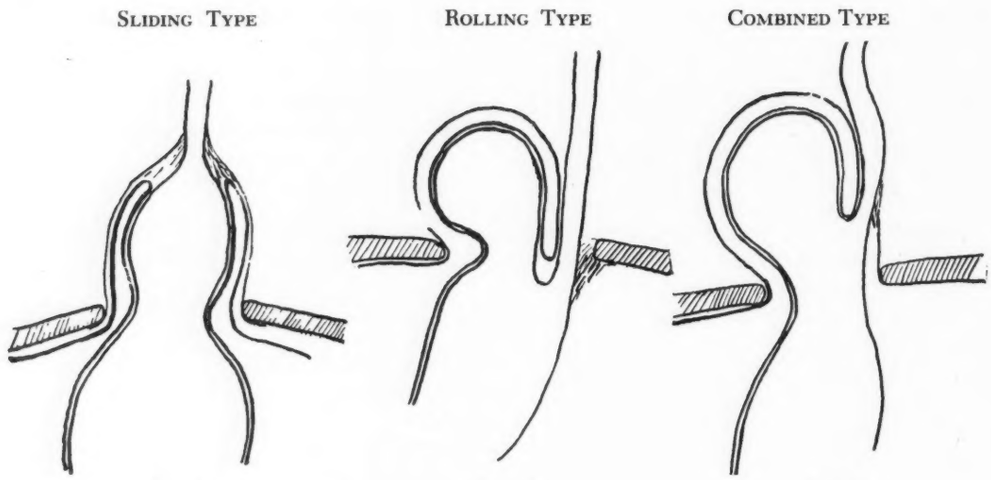

Fig. 4 Fig. 5 Fig. 6

Fig. 4.—Sliding type of hiatus hernia. **Fig. 5.**—Para-œsophageal hiatus hernia. **Fig. 6.**—Composite sliding and para-œsophageal hiatus hernia.

tion is one of the causes of feeding difficulties in babies. Gastric juice regurgitation may cause stricture in these babies, producing organic œsophageal obstruction.

Pregnancy may also be a factor, with raised intra-abdominal pressure and general laxity of all fibrous tissue (Dutton and Bland[5]). In some patients the condition is discovered during or shortly after pregnancy and may be one of the causes of vomiting in the late months of pregnancy. A barium meal is indicated for a pregnant woman who has persistent excessive vomiting in the latter months of pregnancy. Some of the dyspepsia and heartburn found at this period may be caused by œsophageal reflux due to an incompetent œsophageal hiatus. Old age may also be a factor, with the loss of retroperitoneal fat and degeneration of muscle and fibrous tissue around the hiatus.

TYPES

Allison[2] has well described the three types of hiatus hernia and the associated symptoms and signs. The commonest type is the sliding hiatus hernia in which the cardia slides up through the hiatus, carrying a tent of peritoneum with it (Fig. 4). The stomach thus dangles from the lower end of the œsophagus like a bell, so that all obliquity of the cardia is lost as well as the pinchcock action of the hiatus and the ball-valve action of the fundus. Therefore gastric contents may freely regurgitate into the œsophagus on effort or on bending over, as in doing up a shoelace. The œsophageal mucosa is ill-equipped to withstand the irritating effect of being bathed in gastric juice and reacts accordingly with œsophagitis. Patients therefore complain of regurgitation. At night they may wake up and choke, gastric contents regurgitated into the pharynx being aspirated into the trachea so that recurrent lung infection may result. Œsophagitis will produce retrosternal burning pain, which the patient will call heartburn. The œsophagitis may cause ulceration of the lower third of the œsophagus from which continued oozing of blood may occur, producing secondary anæmia. With attempts at healing of the œsophagitis, fibrosis may occur, followed by stricture. Peri-œsophagitis may cause fixation of the œsophagus and stomach in the chest, so that a hernia that was once a sliding variety may become a fixed one. These events may produce shortening of the œsophagus, so that the condition may be mistaken for a congenitally short œsophagus, which, however, is a rare condition.

The second type of hernia is the para-œsophageal variety (Fig. 5). In this the cardia remains fixed below the hiatus, but a hernial sac exists in front of and on the lateral side of the lower œsophagus extending through the diaphragm. Into this the fundus of the stomach rolls, so that the stomach bubble lies above the diaphragm. In this type of hernia the cardia is competent. Therefore there are no symptoms of regurgitation, and œsophagitis does not occur. The symptoms are due to distension of the fundus and inability to empty it by belching. Thus after a meal the patient develops a retrosternal aching pain and has difficulty in belching up wind. Relief of the pain occurs with belching. The intrathoracic fundal pouch is prone to ulceration from which severe bleeding may occur. This bleeding may be aggravated by some obstruction of venous return from this part of the stomach due to compression of the veins by the hiatal orifice, especially as the distension in the fundus increases. It is therefore evident that the sliding hiatus hernia is the hernia of regurgitation, œsophagitis and stricture formation. The para-œsophageal hiatus hernia is the hernia of fundal distension and severe hæmorrhage. It is evident that left phrenic crush may help the former but it is definitely contraindicated in the latter as it may aggravate the condition.

The third type of hiatus hernia is a combination of the sliding and para-œsophageal varieties and may be called the "composite hernia" (Fig. 6). In this type, the cardia and fundus of the stomach both slide up through the hiatus but maintain their natural relationship one to the other. Therefore the œsophagus still enters the stomach at an acute angle, and the stomach bubble still lies above the cardia, but the pinch-cock action of the crura is lost. However, because of the obliquity of entrance of the œsophagus at the cardia, competence is usually maintained, and therefore regurgitation and œsophagitis are not a feature of this third type. Indeed, symptomatically, it is indistinguishable from a para-œsophageal hernia.

DIAGNOSIS

The diagnosis of hiatus hernia and differentiation of the appropriate type hinge on the history and the results of radiological examination with barium and of œsophagoscopy. Physical signs have no part to play. This history has already been discussed in reference to the various types of hernia, but may be summarized as follows: The patient is most commonly a middle-aged to elderly, multiparous female, with a long history of epigastric or retrosternal discomfort or pain related to meals or effort. Flatulent dyspepsia is common. Heartburn, waterbrash, or frank dysphagia is common. Regurgitation on effort and nocturnal regurgitation associated with recurrent pulmonary infections may be noted. A long-continued anæmia due to steady slight blood loss may occur. Frank severe hæmatemesis may also occur.

A radiological examination of the œsophagus and stomach with barium is the single most useful diagnostic procedure. This will be effective in demonstrating hiatus hernia in about 80% of cases provided certain precautions are taken and certain manœuvres are carried out (Palmer[6]).

The relationship of the stomach bubble to the diaphragm must first be defined. Absence of a stomach bubble is strongly suggestive of a sliding hiatus hernia. The radiologist may give the patient an effervescent powder such as soda bicarbonate, or seidlitz powder, to show up this bubble. In the absence of œsophageal stricture, regurgitation of the barium into the œsophagus must be demonstrated to prove a sliding hiatus hernia. This reflux may be produced by such manœuvres as tilting the patient into the acute Trendelenburg position, the Valsalva manœuvre or the raising of the patient's legs off the x-ray table. Of these three, the Valsalva manœuvre is the best. It is very important to obtain spot films of what is seen under fluoroscopy, and above all to obtain good lateral films. In these films it is important to look for the gastric rugæ. If these pass through the hiatus, a hernia must exist. It is also important to define the cardia because the site of this decides whether a Type 1, 2 or 3 hernia is present (Figs. 7, 8, 9).

The finding of a hiatus hernia must not, however, deflect the radiologist from a careful study of the rest of the stomach and duodenum, because duodenal ulcer and hiatus hernia are not uncommonly associated. Furthermore, all these patients should have a cholecystogram done, be-

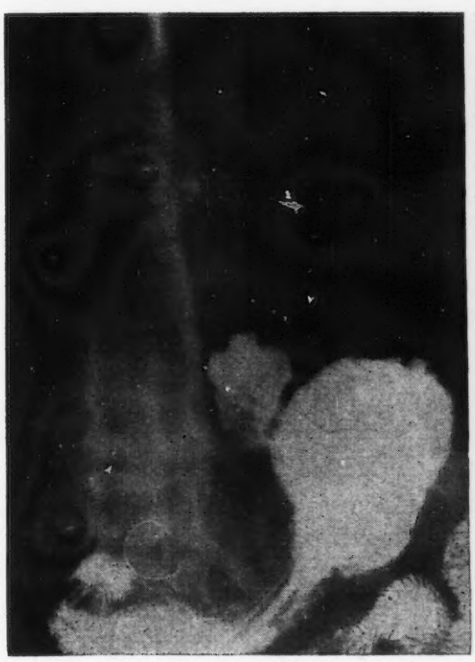

Fig. 7

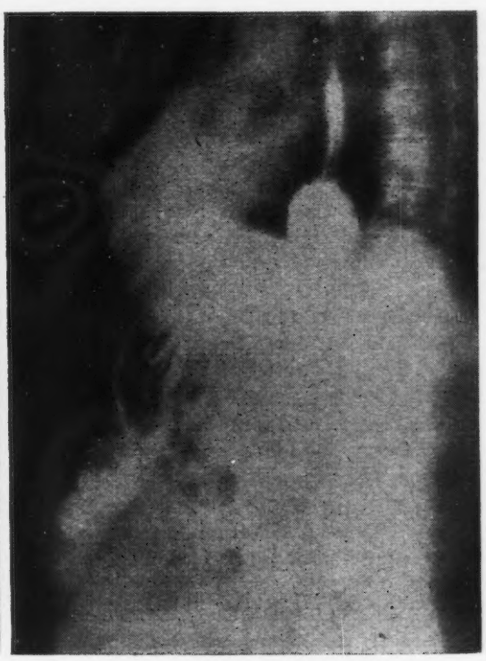

Fig. 8

Fig. 7.—X-ray of typical sliding hiatus hernia showing gastric rugæ passing above the diaphragm. Antero-posterior view. Fig. 8.—X-ray of typical sliding hiatus hernia. Lateral view.

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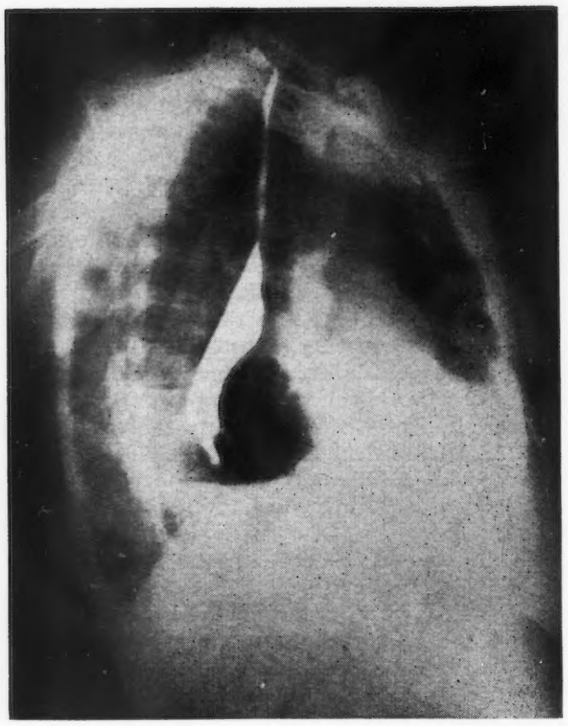

Fig. 9.—Lateral x-ray of combined type of hiatus hernia showing air bubble in fundus in front of œsophagus and above diaphragm.

cause gallbladder disease is a notorious mimicker of hiatus hernia and vice versa.

The third diagnostic procedure is œsophagoscopy. This should be carried out routinely in all hiatus herniæ, preferably by the surgeon interested in the case. The examination should be done on conscious patients under local anæsthesia with adequate pre-examination sedation. It is important to have the patients conscious, so that they may carry out deep inspiration and expiration while the examiner watches the action of the crura through the œsophagoscope, and also so that they can carry out the Valsalva manœuvre and any reflux be noted. Allison[2] made an important point, namely, that a 53 mm. œsophagoscope be used so that no doubt may be entertained that the cardia has been reached and seen. This is not always possible with a 45 mm. œsophagoscope. Although not always easy, it is generally possible to define the œsophago-gastric junction and to measure the distance of this from the upper incisor teeth. The state of the mucous membrane of the œsophagus is seen so that œsophagitis, œsophageal ulcer and stricture can be diagnosed. A biopsy of the mucous membrane may be useful for two reasons. (1) It will show the true state of the mucous membrane. (2) In cases of doubt, it will give the exact site of the cardia, a piece of gastric mucosa being obtained from the area. Another useful manœuvre is to test the mobility of the distal œsophagus by moving the œsophagoscope from side to side; fixity of the lower œsophagus suggests marked peri-œsophagitis and would suggest the advisability of using a transthoracic type of repair. It is obvious that para-œsophageal hiatus hernia will not have any characteristic œsophageal features.

The final diagnostic procedure required for all cases of hiatus hernia is an electrocardiogram. This is necessary because hiatus hernia may well mimic coronary artery disease which, therefore, must be excluded as a cause of the patient's symptoms.

TREATMENT

The treatment required depends on the severity of the symptoms and the general condition of the patient. Many of these patients are essentially symptomless and therefore require no treatment. Others have minimal symptoms which are not worthy of serious treatment. Those with mild to moderate symptoms should be treated medically. Medical treatment consists of neutralization of the irritating effects of gastric regurgitation, since it cannot affect the mechanical defect. The patient is advised to sleep propped up on pillows to reduce nocturnal regurgitation. Pro-Banthine (propantheline bromide) may be tried. A bland Sippy-type diet is prescribed, with appropriate antacids. This regimen may control symptoms in many sufferers. However, œsophagitis, œsophageal ulceration, persistent secondary anæmia and hæmatemesis call for surgical correction. It should be pointed out that para-œsophageal hiatus hernia is not amenable to medical therapy.

Poor-risk elderly patients with a sliding hiatus hernia may be helped by a left phrenic nerve section through a supraclavicular incision.

However, the ideal to be aimed at is the anatomical repair of the hernia. Much has been written recently on the subject. Harrington,[7] in reviewing his series, unfortunately paid scant attention to the anatomy of the area and hence showed methods of repair that are a direct flouting of the functional aspects of the normal hiatus. Allison[2] has had the most beneficial effect on directing surgical opinion to a logical method of repair. A certain recurrence rate must be accepted because so often one is dealing with poor, atrophic, degenerate tissues, but the aim of treatment should be to reduce this recurrence rate to an acceptable minimum.

Of recent years it has become fashionable to suggest that the only legitimate route for repair of a hiatus hernia is via the left lower thoracic approach. Collis, Kelly and Wiley[4] have advocated an abdomino-thoracic approach. This represents an undue swing of the pendulum. Undoubtedly some hiatus herniæ are best repaired through the thorax, while it may be said equally well that others are best repaired via the abdominal route. The surgeon who undertakes to operate on this condition, therefore, should be conversant with both routes and choose the one best suited to the individual patient. What, then, are the factors which dictate which route should

be used? The thoracic route should be used in patients who have a sliding type of hernia which has become fixed by peri-œsophagitis or ulceration, in which difficulty is anticipated in drawing down the œsophagus. A large fixed para-œsophageal hernia, especially if it contains a gastric ulcer or a carcinoma, is another type for the thoracic approach. The habitus of the patient may also influence the route; a hernia in a short, stocky, obese patient may be better dealt with via the thorax.

On the other hand, the abdominal approach is best for the ordinary sliding hiatus hernia with a mobile œsophagus. Any patient who has gallbladder disease, or in whom sub-diaphragmatic lesions exist, should be operated on abdominally.

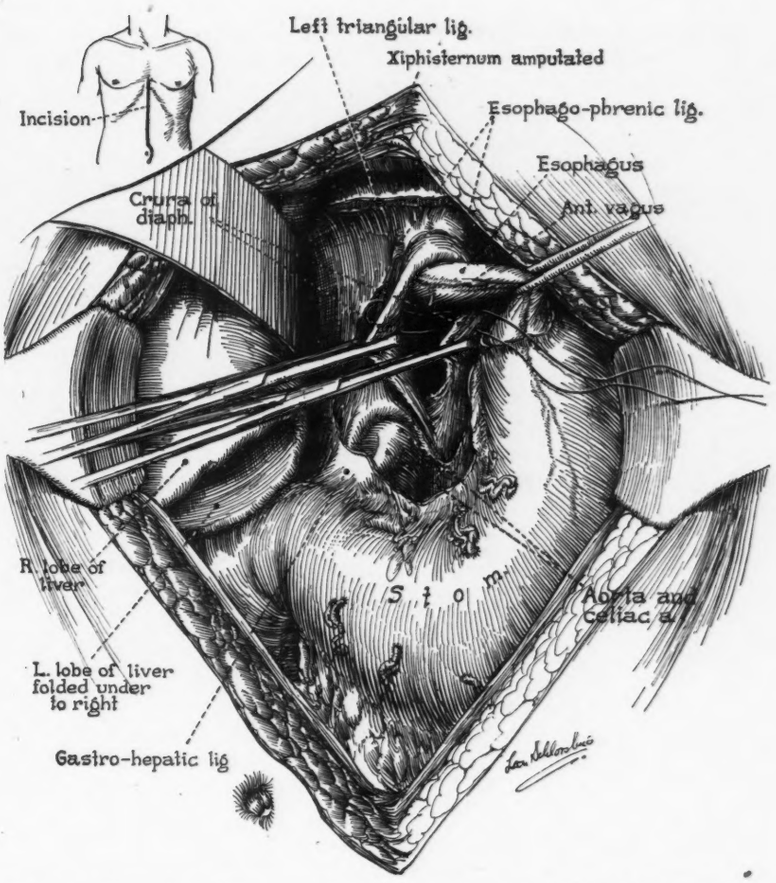

Fig. 10.—First stage of the repair of a hiatus hernia by the abdominal route.

TECHNIQUE

Transthoracic approach.—The patient is placed either in the left lateral or prone position. Holmes Sellers favours the latter. The chest is opened through the bed of the eighth rib or the seventh intercostal space. The lower lobe of the left lung is retracted medially and the inferior pulmonary ligament divided. This gives direct access to the lower œsophagus, which is mobilized from its bed and elevated with a soft rubber sling, such as a piece of Penrose tubing. The stretched œsophago-phrenic ligaments are then divided at their diaphragmatic attachments around the dilated hiatus, and the pouch of the peritoneum drawn up by the œsophagus is also divided around the hiatus. In this manœuvre the upper surfaces of the crura surrounding the hiatus are thus displayed clearly. A radial incision is then made in the diaphragm extending from the dome radially to the lateral chest wall in the line of the muscle fibres, the phrenic nerve being carefully avoided, and the upper abdominal cavity is then entered anterior to the spleen and lieno-phrenic ligaments. The stomach is drawn down through the hiatus, and the lower one inch (2.5 cm.) of œsophagus encircled with another rubber sling so that the cardia can be drawn well down through the hiatus. Three or four sutures of 2/0 silk are placed through the œsophageal attachments of the œsophago-phrenic ligaments, good bites of the fascia propria of the œsophagus being taken, and these are then passed through the hiatus and drawn up through the incision of the diaphragm. The crura of the diaphragm are then approximated behind the œsophagus by interrupted mattress sutures of 2/0 silk inserted from the upper or thoracic surface. These are so placed as not to strangulate the muscle fibres of the crura. The œsophagus then passes through the hiatus at its most anterior and superior point: the hiatus is narrowed down by closing the hiatus in a linear manner behind the œsophagus, the line of closure being antero-posterior. The closure should be sufficiently tight to admit the tip of the surgeon's finger alongside the œsophagus, in the lumen of which passes a No. 18 Levin tube. The lowermost suture, which approximates the origin of the crura as closely as possible, is vital, as it brings the fibres of the two crura parallel to each other. After this, the sutures through the œsophago-phrenic ligaments are passed on a needle through the under-surface of the diaphragm as close to the hiatus as possible and tied, thus tacking the œsophagus to the under-surface of the diaphragm. Two or three sutures attach the fundus of the stomach to the under-surface of the diaphragm lateral to the hiatus as an added security to maintaining the stomach below the diaphragm. The incision in the diaphragm is closed by interrupted silk sutures. The thoracic cavity is then closed without drainage.

The method described above is essentially that described by Allison.[2] However, some surgeons are unimpressed with the necessity of repairing the œsophago-phrenic ligaments, or suturing the fundus of the stomach to the under-surface of the diaphragm. These surgeons therefore do not open the diaphragm, but push the stomach and cardia down through the hiatus and merely suture the crura. This would appear to be an inadequate operation in so far as this is a hernia in which recurrence is known in an appreciable percentage of cases, and therefore any logical ancillary proceeding which may help to prevent this would appear to be justified.

Abdominal route.—The abdomen is opened through an upper midline incision. The exposure can be greatly facilitated by excising the xiphisternum. The abdomen is explored for lesions other than the hiatus hernia, special attention being given to the gallbladder and duodenum. The triangular ligament of the left lobe of the liver is then divided, and the left lobe is folded under and medially and held there by a retractor. This gives an excellent exposure of the œsophageal hiatus. This hiatus is then explored with the finger. The size of the defect and the extent of the hernial sac are defined. The stomach is then drawn down. The peritoneum over the anterior aspect of the œsophagus is divided as in the operation of vagotomy, and the lower œsophagus thereby defined. A finger is passed round the œsophagus and a rubber Penrose sling passed round

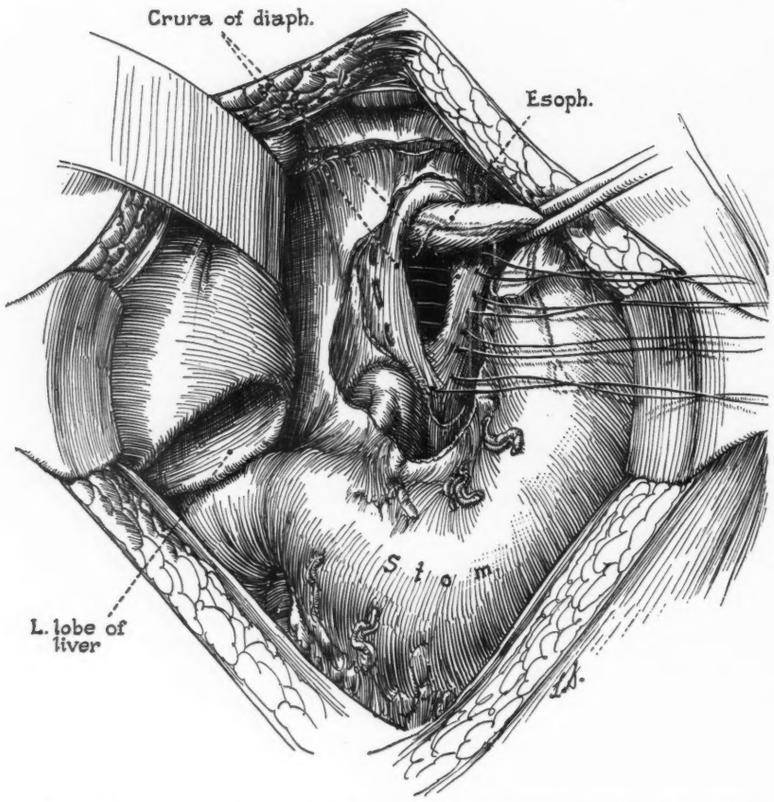

Fig. 11.—Repair of hiatus hernia by the abdominal route. All sutures are passed before they are tied.

it, the sling thereby drawing on the crutch between the œsophagus and the fundus of the stomach at the cardia. In the case of a para-œsophageal hiatus hernia, the peritoneal sac is incised at its neck at the hiatus, and the sac is readily drawn down out of the posterior mediastinum, much as a urinary vesicular diverticulum is removed by a transvesical approach. The dissection of the peritoneum over the crura is then carried distally till the whole of the crural muscle fibres can be clearly seen down to the median arcuate ligament, which is that aponeurotic portion of the diaphragm arching over the aorta just proximal to the origin of the cœliac axis artery. The crura are then picked up with long tissue forceps, of the Allis or Littlewood type, one on each crus, a manœuvre which makes the suturing of the crura simple (Fig. 10). Horizontal mattress sutures are then passed through these crura, using 2/00 silk. All sutures are passed before any are tied (Fig. 11). The vital and key suture is the lowest one which approximates the origins of the crura and is situated just above the median arcuate ligament. The suture is comparable to the similar one in an inguinal hernia repair which approximates the insertion of the conjoined tendon to Poupart's ligament or Cooper's ligament. Both sutures bring the line of fibres of the respective muscles, viz. the two crura and the conjoined tendon, parallel to each other; in the case of the crura, in an anteroposterior direction, and parallel to Poupart's ligament in the case of the inguinal hernia. The mattress sutures are then tied one at a time commencing from below, and the size of the resulting œsophageal opening is checked by the surgeon's fingertip so that excessive narrowing is not achieved. These vital crural sutures are more readily inserted by the abdominal route than via the thoracic route, because the crura can be more accurately defined by the former route and the vital lower suture can be inserted only by this route. The remnants of the œsophago-phrenic ligaments can now be clearly seen and three or four interrupted 2/0 silk sutures can reattach them to the under-surface of the diaphragm and the hiatus (Fig. 12). It is often advantageous to divide that branch of the anterior vagus nerve passing in the lesser omentum to the liver to get better exposure; no harm results from this. The peritoneum on the anterior aspect of the œsophagus is then resutured to that on the under-surface of the diaphragm, making a third and final line of defence in

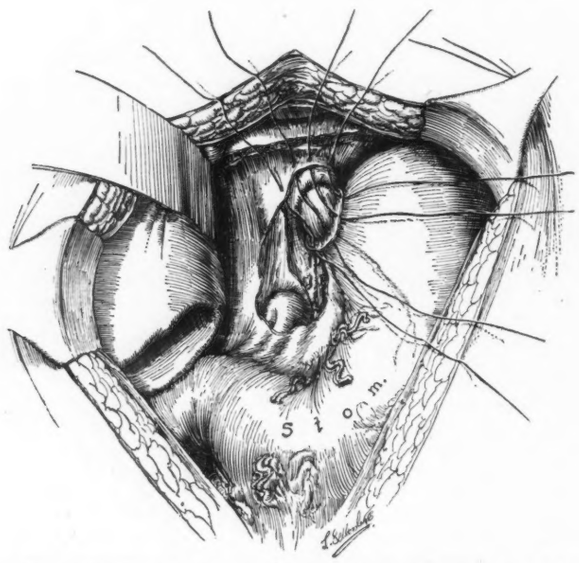

Fig. 12.—Repair of œsophageal hiatus hernia by abdominal route. Stage 3. Œsophago-phrenic ligaments are reconstituted.

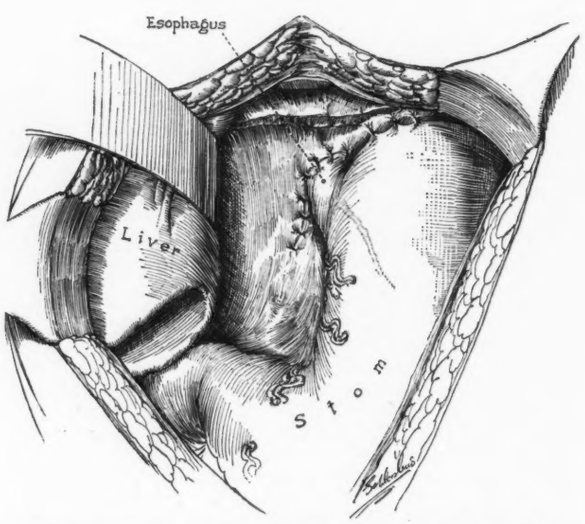

Fig. 13.—Final stage of repair of hiatus hernia by abdominal route.

the repair. A few sutures then attach the fundus of the stomach to the under-surface of the diaphragm, lateral to the hiatus (Fig. 13). The left lobe of the liver is unfolded and returned to its place. Should gallstones be present, a cholecystectomy can now be performed. The abdomen is then closed.

Whichever route is used, it is wise to pass a Levin tube into the stomach before operation to ensure a stomach empty of fluid and air; a fundus distended with air is a distinct disadvantage to the exposure. Furthermore, the tube serves the useful purpose of defining the œsophagus and assists in making sure the hiatus is not closed too tightly. A hiatus which admits the tip of the surgeon's finger as well as a Levin tube will be the correct size.

Postoperatively it is not unusual for some degree of dysphagia to be present for a few days. This may be regarded as a good sign, as it usually indicates adequate closure of the hiatus. As œdema and reaction to operative trauma round the hiatus settle down, the dysphagia goes.

Conclusion

A study has been presented of œsophageal hiatus hernia from an anatomical point of view. The possible etiological factors have been discussed. The types of hernia have been described and the differing symptoms of each have been pointed out. The principle of repair of these herniæ has been outlined to fit in with the anatomical and physiological concepts. An endeavour has been made to revive interest in the transabdominal repair of these herniæ.

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MISCELLANY

"I BEQUEATH MY BODY TO SCIENCE"

Occasional requests for information are received at C.M.A. House from solicitors and others interested in the proper procedure for willing a human body "to science" or "for the advancement of medical knowledge". It is possible that practising physicians may also receive such enquiries and they may be interested in an authoritative statement on the subject.

We are indebted to Dr. J. C. B. Grant, Professor of Anatomy, University of Toronto, for providing the material which is produced hereunder. It is emphasized that the statement of the legal position applies specifically to the Province of Ontario and doctors resident elsewhere should satisfy themselves of the regulations which apply in their province. The supply of human subjects for anatomical dissection is verging on the inadequate in many Departments of Anatomy at Canadian universities, and doctors should not discourage patients who are disposed to bequeath their bodies.

Anatomical subjects should preferably not be embalmed by the methods usually employed by undertakers, and if an autopsy is indicated, the Department of Anatomy is usually prepared to carry it out and to report the findings.

Information on the Bequeathing of One's Body.

If you wish your body after your death to be bequeathed to a Department of Anatomy, which is the only place where it can be held legally, then the approved procedure to follow is to advise your lawyer of your wish and to have it stated definitely in your will to the following effect:

> "Upon my death I direct that my body be delivered to the Department of Anatomy of the University of ..... (or to the nearest Medical School) according to the provisions of the Anatomy Act (Ontario), and in the event that this direction cannot be carried out by my executor or if my body is not in suitable condition for use by the medical school, then my executor shall dispose of my body as he may see fit."

As it is usual not to read a will until after burial, it is well that during your lifetime a relative, your doctor, and your lawyer (and your clergyman, if you so desire) should know of your wish (to have your body used for the advancement of medical science) so that, at the time of your death, your wish may be carried out; it is too late to make this known when one's will is read after one has been buried.

It is desirable that these people should have been informed of your wish previously, for at the time of your death they should notify Dr. Smirle Lawson, 86 Lombard Street, Toronto 1, Ontario, immediately. As Inspector General of Anatomy and Chief Coroner of Ontario, Dr. Lawson will arrange a suitable disposal.

Since you may not know, it is well to add that it is illegal to traffic in human bodies, and therefore no sum of money can be advanced to those so generous as to bequeath their bodies, or to their estate or to any relative or other person.

Ultimately a Christian burial will be arranged by the proper authorities, who will pay the cost. There will be no charges against the estate or any relative, and no reference will be made to the next-of-kin when the burial is taking place unless the Department is requested to do so. A service is conducted by a clergyman in the presence of one or more members of the staff of the Department of Anatomy.

HÆMODIALYSIS FOR ACUTE BARBITURATE POISONING

Berman and his colleagues from Washington, D.C., (*J. A. M. A.*, 161: 820, 1956), make a plea for the use of the Kolff artificial kidney in the treatment of acute barbiturate poisoning. They have treated eight cases in this way, and followed up the removal of the barbiturate from the circulation quantitatively throughout dialysis. The highest concentration found initially in the blood was 29 mg. of barbiturate per 100 ml.; in one case dialysis removed more than 9 g. of phenobarbital from the body (37% of the ingested dose).

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GENERAL PRACTICE

A GENERAL PRACTITIONER'S POSTGRADUATE EDUCATION

DR. J. E. HUDSON has recently completed a course of study at Cook County Postgraduate School of Medicine, Chicago. This course was made possible by a grant given by the Manitoba Institute for the Advancement of Medical Education and Research, and Dr. Hudson was chosen to be the recipient of the grant by a committee appointed by the College of General Practice of Canada. Cook County Postgraduate School of Medicine has existed since 1932 and operates under the supervision of the attending staff, who are also members of adjoining university staffs. With its 3,400 beds, the hospital is one of the largest general hospitals in the world and has an outpatient department handling over 200,000 patient-visits a year. It therefore has a wealth of material for postgraduate teaching.

Dr. Hudson chose an informal course in pædiatrics because the teaching is done at the patient's bedside and not in the lecture room. In his report of his experiences there, Dr. Hudson mentions the very interesting group of resident interns who come from all over the world. He describes in detail two particular features of the pædiatric teaching which impressed him. One was the ward rounds on the premature baby ward, which students visited together with a staff physician. The other was the outpatient clinic for rheumatic fever, where patients who had had rheumatic fever came back monthly to an outpatient clinic and were given long-acting penicillin. Dr. Hudson was also impressed by the very active muscular dystrophy clinic. He also mentioned the daily final conference in which interesting problem cases are discussed by staff physicians, resident interns, and students.

APPROVED GENERAL PRACTICE RESIDENCIES

THE COLLEGE OF GENERAL Practice of Canada is an organization dedicated to broad educational principles aimed at advancing the academic standards of the family doctor. This objective calls for an educational program of many facets. Three of these are:

1. To ensure that members of the College of General Practice engage in postgraduate education to a minimum extent of 100 hours per two-year period.

2. To promote some undergraduate teaching by and for general practitioners, so that those who contemplate this desirable and diversified practice of medicine may be better oriented in their student days. The College believes that more of the training of interns could be in smaller hospitals with family doctors teaching the fundamentals of general medical practice.

3. To encourage the future general practitioner to take the necessary intern and residency training, so that he may capably assume his position in the particular locality in which he may enter practice.

The first facet described above is already being effectively established by the College of General Practice, which has assisted and promoted the presentation of postgraduate programs throughout the Dominion.

The second facet is one which the College is studying and hopes to develop within the next several years. Indeed it is a part of its residency training program.

The third facet is now in the advanced planning stage. Commencing in July 1957, there will be general practice residencies approved by the College in many of the principal hospitals in Canada. This residency training program will be of sufficient duration and educational content to enable the resident on completion of training to begin practice as a more competent family doctor.

An approved residency will consist of the following basic components:

(a) That the intern considering a residency in general practice must first complete a junior rotating internship in a hospital approved by the Canadian Medical Association.

(b) That a second year of residency be arranged to provide the following subjects: (1) Three months of medicine including dermatology. (2) Three months of obstetrics and gynæcology. (3) Three months of general and emergency surgery and fractures, ENT and urology. (4) One month of anæsthesia. (5) Two months of pædiatrics.

(c) That a preceptorship program of training with a senior practising physician be included in or follow the residency training and be a minimal two-week period and preferably four weeks.

The family doctor practising in different communities will have different demands placed on his knowledge. Where special skills beyond the scope of a two-year postgraduate training program are required, it would be hoped that the resident would undertake the necessary training in order that he might rightfully take his place in his particular locality. It is not desirable or essential that all hospitals should have the same program or sequence of experience. Therefore it is readily realized that, in some particular instances, more than one year of residency would be advantageous.

At a recent meeting of the College of General Practice, it was apparent that those physicians who had satisfactorily completed this training would be more suited to general practice and should be so recognized. Therefore it was unanimously approved that one year of approved general practice residency will be considered the equivalent of two years in practice, when an applicant is seeking membership in the College.

In the course of the next few months, the College of General Practice of Canada will publish in this and in other journals a list of those general practice residencies which have been approved. Moreover, with the help of CAMSI and its journal we hope to popularize this program of residency training for general practice.

Thus, in keeping with the basic aims of the College, the principal objective of a residency in general practice is to develop clinical responsibility and sound judgment of the everyday diseases and conditions with which a physician will be confronted in general practice. Further, it is the desire of this program to create in the future family doctor a full awareness of the importance of consultation and/or referral in the difficult or obscure cases with which he may be called upon to deal.

Further information concerning the residency training program may be obtained from: The College of General Practice of Canada, 176 St. George Street, Toronto, Ontario.

DR. N. N. LEVINNE, Chairman,
Committee on Residency Training.

REPORT OF THE COMMITTEE ON EDUCATION

THE PROBLEM OF POSTGRADUATE education – or continuing education of practising physicians—is one of the greatest problems facing us today. We all recognize the fact that medical science has been developing at a very rapid rate, particularly in the past few decades. How to get the practising physician and the recent developments together is the crux of the problem. The new crop of physicians are kept abreast of the newer developments because of their teaching in undergraduate training and in their specialty training. The weak spot seems to be in getting this to the practising men and the men who are actually treating the patients. The general practitioner had nothing but his own initiative to stimulate him to keep up and frequently it was relegated to the category of one of those things he would do next year.

In 1954 the College of General Practice was formed with one of its requirements for membership being 100 hours of postgraduate study in every two-year period. It was felt that this requirement was rugged enough that standards of membership would be maintained at a fairly high level and at the same time was not so high that the majority of men could not qualify if they wished to do so.

Just stating that 100 hours of study were compulsory was not enough. A Committee on Education was appointed to get the answers to several questions that had to be considered, such as "What courses are available?" "What types of courses would be more attractive?" "Would lectures be better than tape recordings?" "How long should the courses be?" "Should the men in smaller rural areas have different types of postgraduate work available?"

The first thing that was done was to make a list of all available courses with their location—length of time—approximate cost—and this has been published from time to time in our News Bulletin.

In an attempt to answer most of the other problems, a questionnaire was prepared and sent to all members of the College in 1955. One thousand and thirty of these were sent out and 664 replies were received, which thus gave a good cross-section of opinion, as they were representative of all parts of Canada.

Some very definite conclusions can be drawn from the replies.

1. It was quite obvious that by far the majority of members prefer postgraduate courses at main centres.

2. It was very obvious that by far the majority prefer courses of one week or less (approx. 90%) and of these nearly two-thirds prefer courses lasting not more than three days (this is in keeping, I believe, with the A.A.G.P., who have found that courses of one week or less are most desirable). One interesting point here was that the six-day courses are the most popular in rural areas, differing statistically in a significant manner from the university centres, where the three-day courses are the most popular.

3. The second most desirable type of postgraduate education is that of travel teams.

4. It was quite obvious that travel teams staying in a community for two to three days and doing ward rounds, and helping in discussions of local problems were preferred to a team with a set number of formal lectures. This type of postgraduate instruction, as might be expected, was much more desired in rural areas, presumably because people in rural areas cannot readily leave their practices. They ask that more teaching should be brought to them.

5. The third most popular type of postgraduate instruction was the scientific sessions held at annual provincial or national meetings.

6. Reading courses and tape recordings ranked fourth and fifth respectively but away down in popularity.

Thus we now know what the general practitioners prefer—both as to type of postgraduate education and as to how long they like the courses to be. We also recognize that there is a demand for travel teams to go into a rural community for 2-3 days and work with the men and discuss difficult cases and demonstrate diagnostic procedures, e.g. proctoscopic examinations, etc., as has been done in several places very successfully.

Reading courses and tape recordings, despite our previous opinions, did not rank very high, although it is quite possible that well-organized reading courses, in particular, could be a big help to men in isolated areas who find it difficult to get away. However, it is rather felt that the percentage of men working alone is becoming smaller as group practice becomes more prevalent, and this makes it easier for a man to undertake postgraduate work.

It would seem that the interest in and demand for postgraduate training is increasing steadily and it becomes more essential as medicine progresses more rapidly. It seems realistic that postgraduate courses for general practitioners should be provided by specialists in consultation with the men in general practice. That is, the general practitioners should arrange the courses and decide what they want to know and how long a course they are anxious to undertake, etc. The majority of lectures and courses are given by specialists and should be, as they are each experts in a particular line. However, they do not always have a clear concept as to what the man in general practice wants to hear about. Many

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lectures tend to be similar to lectures given to undergraduate medical students. At that stage one is inclined to be more interested in a very rare brain tumour or in a long, complicated, new method for doing a cardiac surgical procedure. However, after one has been out in practice for a few years one becomes much more interested in more common illnesses and procedures that one sees frequently, and in how to recognize the somatic from the psychic elements in a particular case. Points of detail that to a medical student may have been remote and disjointed facts often "ring a bell" in the mind of a practising physician who has need of that particular information. The physician's frame of reference is entirely different from that of the medical student. He tempers pure fact with judgment and he constantly thinks in terms of practical applications rather than in terms of the probability of an item turning up on an examination. His practice has shown him his weak points and he is on the lookout for material that will meet his own particular needs.

It would seem apparent that this leads to the confusion in many minds between postgraduate education and graduate education as at present existing. The latter is usually a specialized training towards a specialty training in a particular field—whereas postgraduate education, as we hope it will be arranged, is primarily for the purpose of keeping physicians abreast of their own field of practice or expanding their knowledge of one aspect of it. The major purpose as stated earlier should be that of bridging the gap between medical research and medical practice. This, in turn, will aid in raising the general level of medical practice, and certainly if we had to state one main objective in forming the College of General Practice, it is that of raising the general level of medical practice so that we can provide better medical care for the people of Canada.

In conclusion, we should each remember that provision of courses and organization of the College means nothing unless we as individuals take an interest in keeping up to date and recognize that it is essential that we do so. It has been stated that physicians need to be refreshed in all aspects of medicine every four to five years, so we must realize that to do so properly requires considerably more than 100 hours every two years for a man in general practice. This is a bare minimum. It is up to each of us personally to take frequent postgraduate courses and to make our desires known to the teachers in our profession. In this way we will ensure our fitness to practise medicine of the highest possible calibre.

It is the hope of the College of General Practice to stimulate the Provincial Chapters to ensure provision of good postgraduate education of various types in all the provinces of Canada.

April 1956. E. C. McCoy, M.D., Chairman.

MEDICAL MEETINGS

CANADA'S THIRD MEDICAL CARE CONFERENCE

Judging by the quality of the papers presented and the increased attendance, Canada's third Medical Care Conference, held in Saint John, N.B., May 31 and June 1, in conjunction with the Annual Meeting of the Canadian Public Health Association, was an unqualified success.

Such conferences are designed to serve as a forum for bringing together representatives of all those groups with an important interest in the field of hospital and medical care, including medical and hospital organizations, administrators of government health programs, voluntary prepaid medical and hospital plans, insurance companies and others with a substantial interest in the teaching and research aspects. A series of papers is prepared and delivered each year by recognized leaders in their respective fields, after which open discussion by those in attendance takes place. While no conclusions are drawn, the broadening influence of many viewpoints tends to aid in the development of an increasing pool of well-informed opinion useful to all concerned in this important field of human endeavour.

The program at this year's conference included the following: "Some Patterns of Medical Care from the Canadian Sickness Survey"—R. Kohn, Ph.D., Chief, Public Health Studies, Statistics Section, Health and Welfare Division, Dominion Bureau of Statistics, Ottawa. Panel Discussion, "Proposed Federal-Provincial Hospital and Diagnostic Services Program"—Mr. J. Sparks, Research and Statistics Division, Department of National Health and Welfare, Ottawa; Dr. M. I. Roemer, Director of Medical and Hospital Services, Provincial Department of Public Health, Regina; and Dr. J. S. Roberston, Deputy Minister of Health, Nova Scotia. "The Place of Medical Co-operatives in a Complete Health Plan"—Mr. Alex Laidlaw, Associate Director, Extension Department, St. Francis Xavier University, Antigonish, N.S. "A Board Chairman Examines Principles of Responsible Trusteeship of a Typical Blue Cross–Blue Shield Plan"—Dr. J. A. MacDougall, Board Chairman, Maritime Hospital Service Association, Saint John, N.B. "Hospital Insurance Service Plan Administrator Examines Principles of Responsible Management"—Miss Ruth Wilson, Executive Director, Maritime Hospital Service Association, Moncton, N.B. "Prepaid Medical and Hospital Care by the Check-Off System in Cape Breton"—Dr. H. J. Devereux, Chairman, Medical Economics Committee, Medical Society of Nova Scotia. "Recent Developments in Group Health Insurance"—Mr. Carman Naylor, Associate Group Actuary, London Life Insurance Company, London, Ont. "Merits and Demerits of a Plan for Prepayment of Medical Care under a Physician-Sponsored Agency"—Dr. J. F. L. Woodbury, Chairman, Committee Studying Relationship between Maritime Medical Care and the Medical Society of Nova Scotia, Halifax, Nova Scotia. "Medical Services in the Nova Scotia Department of Welfare"—Mr. F. R. MacKinnon, Director of Child Welfare and Mothers' Allowances, Nova Scotia Department of Welfare, Halifax.

As a result of a resolution passed at the previous conference a year ago in Edmonton, Alta., requesting the establishment of a medical care section of the Canadian Public Health Association which would be designed to give permanence to such a type of gathering, such action was taken and the first meeting of the Medical Care Section of the Canadian Public Health Association was held, at which time the following slate of officers were elected: Chairman: Dr. B. H. G. Curry, Ontario Workmen's Compensation Board; Vice-Chairman: Mr. D. N. Cox, Commissioner, British Columbia Hospital Insurance Service; Dr. Jules Gilbert, School of Hygiene, University of Montreal; Dr. G. Graham Simms, Assistant Deputy Minister of Health, Nova Scotia; and Mr. C. Howard Shillington, Executive Director, Trans-Canada Medical Plans; Secretary: Mr. John E. Osborne, Research Division, Department of National Health and Welfare, Ottawa.

At the concluding business session of the conference, a resolution was passed recommending that one of the functions of the Medical Care Section of the Canadian Public Health Association be to hold a Medical Care Conference annually, open to all interested persons regardless of their membership in the C.P.H.A.

It was also agreed that the small remaining bank balance belonging to the Conference be passed to the Secretary of the Medical Care Section for the purpose of promoting future meetings of the Section and paying for mimeographing and distribution of the papers presented to all members of the Conference.

With this action the existence of the Medical Care Conference as an individual entity was brought to a close, with the hope that from its excellent beginnings there would develop, on a more permanent basis, larger and even more successful conferences. C.H.S.

CANADIAN OPHTHALMOLOGICAL SOCIETY

The 19th Annual Meeting of the Canadian Ophthalmological Society was held at the Château Frontenac in Quebec City in June 1956. Dr. John McLean of Vancouver was in the Chair in the absence of the President, Dr. Henri Pichette, who was ill.

At this meeting there was considerable discussion of the development of eye banks in Canada. The distinguished Managing Director of the Canadian National Institute for the Blind, Colonel E. A. Baker, was made an Honorary Member and addressed the Society briefly.

Dr. J. H. Grove, the Chief of the Division of Blindness Control of the Department of National Health and Welfare at Ottawa, was made an Associate Member. Dr. Grove expressed the desire of his Department to work together with the ophthalmologists in solving visual problems.

The Society was honoured by the visit of two distinguished ophthalmologists from abroad, Dr. Moacyr Alvaro of Sao Paulo, Brazil, and Mr. H. E. Hobbs of London, England. Dr. Alvaro gave a most illuminating paper on "The Results of Organized Ophthalmology in the Americas". Mr. Hobbs gave a paper on "Visual Field Defects in Chiasmal Lesions" and contributed much in the discussion of other papers.

Dr. Paul Chandler of Boston was the guest of honour and he gave two papers, one on "Angle Closure Glaucoma" and one on "Complications of Congenital Cataract Surgery". These papers, of course, were presented in such a lucid and interesting way that they contributed greatly towards a very successful meeting. The Society is much indebted to Dr. Chandler for taking the time to come to the meeting.

Papers by the members covered nearly every branch of ophthalmology. All the papers will appear in the Transactions of the Canadian Ophthalmological Society.

Dr. John McLean of Vancouver was elected President for the coming year and will preside at the next Annual Meeting, which will be held at Banff in June 1957. Dr. J. V. V. Nicholls of Montreal was elected Vice-President. Dr. J. Minnes of Vancouver was elected a member of the Council. The Secretary, Dr. R. G. C. Kelly of Toronto, the Treasurer, Dr. B. Alexander of Montreal, and the Editor-in-Chief of the Transactions, Dr. Clement McCulloch of Toronto, were re-elected.

HOW MANY CALORIES?

How many calories do you really expend in present-day life? With automation at work, with more people riding cars than bicycles, with all the hours spent at "do-it-yourself" projects, and other hours spent slumped in front of television, with all the calories from cocktails, and all the other calories you ingest, what sort of balance is needed? Questions of this type were considered by a Committee convened in Rome by the Food and Agriculture Organization of the United Nations to revise the First Report on Calorie Requirements issued in 1950. The Second Report should be off the presses in a few months.

The 11 persons on the Committee included physiologists, biochemists, a consumption economist, and Dr. Pett of Canada as a public health nutritionist. Eight countries were represented. The First Report on Calorie Requirements was considered in 1955 by a Joint FAO-WHO Committee to be "sound and workable", especially for its primary purpose of evaluating in calories the national food supplies around the world, but to need review and revision.

A feature of the 1950 Report is the use of a "reference man" and a "reference woman" of stated size, activity, etc., and judged to need 3,200 calories and 2,300 calories daily respectively. These references are continued in the Second Report. Since 1950, various investigators have advanced our knowledge of actual energy expenditure at different activities, whether at work or non-occupationally. To a considerable extent it is now practicable to consider the energy requirements of people for any one day under three headings: (1) resting in bed; (2) at work; (3) in non-occupational activities including sports and transportation. This method of calculating calories requirements by summarizing the day's separate activities is not new, but data have been lacking on which to base it. The Second Report gives it due attention.

The influence of body size on calorie requirements, as used in the Canadian Dietary Standard, is reiterated, but many activities nowadays are not so closely related to body size. For example, consider work that really requires only pulling levers or pushing buttons, or sitting at television, or the extra calories needed to carry heavy objects. The modern system of rest pauses must also be considered in evaluating calorie needs of occupations. A new discussion of such factors will be found in the Second Report.

A critical review was made of the calorie needs of pregnancy, lactation, growth in children, and the influence of age, climate and the character of the diet.

Since the report is primarily to be applied to evaluate the adequacy of food supplies of groups of people, or whole nations rather than individuals, a new section on its application has been written. For the same reason the calories consumed as alcohol are given special attention in this Second Report. Alcohol calories enter metabolism and should be counted, whether or not their source is considered a "food".

For physicians generally, the FAO Report on Calorie Requirements, will still not give figures to apply directly to individuals. Weight control by a balance between a suitable amount of activity and the diet, should be the objective for individuals, and tables of calorie requirements are not easily applicable to them. But the new report, when it becomes available, will list many of the factors that physicians have to consider in relation to the energy cost of growing children, or of lactation, or of different climates, or of different kinds of activity.

L. BRADLEY PETT, Ph.D., .M.D.,
Chief, Nutrition Division,
Dept. of National Health and Welfare,
Ottawa.

AMERICAN COLLEGE OF CHEST PHYSICIANS

The 22nd Annual Meeting of the American College of Chest Physicians was held at the Hotel Sherman, Chicago, Illinois, June 6-10. Over 1,400 physicians and guests attended the meeting. Fellowship certificates were presented to 250 physicians at the Convocation held on Saturday, June 9.

Dr. Henry C. Sweany, Director of Research, Pathology and Allied Sciences, Missouri State Sanatorium, Mt. Vernon, was awarded the College Medal for his outstanding contributions in the field of chest pathology.

The following officers of the American College of Chest Physicians were elected for the year 1956-1957: President, Herman J. Moersch, Rochester, Minnesota; President-elect, Burgess L. Gordon, Philadelphia, Pennsylvania. Dr. T. G. Heaton, Toronto, Ont., was elected Regent of the College for Canada. Dr. L. R. Coke, Winnipeg, Man., was elected Governor for the Western Provinces of Canada.

The following physicians from Canada received their Certificates of Fellowship in the College at the Convocation on June 9: Donald Cant, Corner Brook, Newfoundland; R. H. Craig, Waterloo, Ont.; John A. Lewis, London, Ont.; Gilles C. Lorange, Montreal, Que.; C. W. McCormack, Edmonton, Alta.; A. F. Perl, Sarnia, Ont.; Ernst A. Rohr, Sudbury, Ont.; Samuel Shuster, Montreal, Que.; J. A. Turner, Toronto, Ont.; and Arthur Vineberg, Montreal, Que.

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Executive Committee of Trans-Canada Medical Plans (left to right): Dr. A. G. MacLeod (Honorary Treasurer), Dr. J. A. Ganshorn (Vice-chairman), Dr. G. C. Ferguson (Honorary Secretary), Mr. E. D. Millican, Dr. S. A. Orchard (Chairman), and Mr. C. Howard Shillington (Executive Director).

TRANS-CANADA MEDICAL PLANS

Trans-Canada Medical Plans held its annual meeting at Quebec City on June 8, 9 and 10, just before the opening of the Canadian Medical Association annual meeting. In his annual report, the chairman, Dr. S. A. Orchard, recorded another year of substantial progress for the medically sponsored prepaid medical care plans across Canada. There was a net increase of 319,309 persons enrolled and this was the greatest single year of growth in the five-year history of T.C.M.P. The total enrolment was now 2,400,000. The chairman noted the extension of coverage, with particular reference to small groups in which an employer had only three to nine employees and in connection with rural farming communities. The administration costs of medical plans had been held to below 9%, some 90% going to the actual payment of claims.

The need for the future, said the chairman, was to continue rapid expansion of member plans to meet the needs of those still uncovered, particularly among the rural population, retired groups, individual shopkeepers and other persons. It had been suggested that voluntary plans would not be able to meet public demand quickly and adequately enough, and therefore that a state-operated program was essential to Canada. Nevertheless, this was not borne out by the fact that quite a large section of the population did not appear to want a universal compulsory health insurance. The second responsibility of the medical care plans was to continue to bridge the gap between advances in medical knowledge and their application to individual needs. Finally, the public must be assured of the continuance of efficient and economical operation of the plans. The chairman stressed once again that the greatest assets of the nation were still individual initiative and responsibility, each of which is adequately reflected in the voluntary health movement.

The members of the Executive Committee of Trans-Canada Medical Plans are Dr. A. G. MacLeod (Honorary Treasurer), Dr. J. A. Ganshorn (Vice-chairman), Dr. G. C. Ferguson (Honorary Secretary), Mr. E. D. Millican, Dr. S. A. Orchard (Chairman), and Mr. C. Howard Shillington (Executive Director).

NIAGARA FALLS MEDICAL ASSOCIATION

The annual Clinic Day of the Niagara Falls Medical Association will be held at the Sheraton-Brock Hotel, Niagara Falls, Ont., on Saturday, September 15, 1956. The speakers will be Dr. W. T. Mustard and Dr. K. J. Wightman of Toronto; Dr. Earl Plunkett of London, Ont., and Dr. Stanley Hoerr of the Cleveland Clinic.

CORRESPONDENCE

RADIOGRAPHS OF EX-SERVICE PERSONNEL

To the Editor:

A fact that is not generally known by practising physicians and hospital staffs is that previous x-rays of patients who have served in the Army, Navy or R.C.A.F. can be obtained by a doctor by writing to: Department of Veterans Affairs, Central X-Ray Film Library, Ottawa, Ont.

In writing for these x-rays, it would be necessary to include the patient's former service number, rank, full Christian names, and branch of service at time x-rays were taken. These x-rays are often valuable for comparison, follow-up studies and investigation of old or new complaints.

J. I. LEESON, M.D.,
Squadron Leader,
Senior Medical Officer.

R.C.A.F. Station,
Saskatoon, Sask.,
June 28, 1956.

SPECIAL CORRESPONDENCE

The London Letter

(From our own correspondent)

Nuclear Radiation Hazards

The Medical Research Council report on "The hazards to man of nuclear and allied radiation" covers a wide field, taking in its stride illuminated watches, shoe-fitting x-ray sets, and television, as well as atom bombs, diagnostic radiology and radiotherapy. So far as the explosion of nuclear weapons is concerned, anxiety is expressed at the possible harmful effects of radiostrontium in the fall-out. The possibility cannot be ignored that, if the rate of firing increases, and particularly if greater numbers of thermonuclear weapons are used, we could within the lifetime of some now living be approaching levels at which ill-effects might be produced in a small number of the population. On the bases that "there is a limit to the amount of radiation which any population or any individual can accept" and that "we cannot afford to expend, without careful forethought, the margin which is now available to us", various recommendations are put forward for reducing the risk from radiation from other sources. These recommendations include a revision of present practice in medical radiology, and of certain uses of radiation in the treatment of non-malignant conditions, particularly in children. The hope is also expressed that the use of x-rays in shoe-fitting will be abandoned except when prescribed for orthopædic reasons, and that watches and clocks with radioactive luminous dials will be confined to necessary uses. So far as television is concerned, whilst the radiation hazard is at present negligible, the position may change if special types of highvoltage equipment come to be widely used.

The Poliomyelitis Vaccination Campaign

The Ministry of Health has already run into minor difficulties in the current poliomyelitis vaccination campaign. The first was that two cases of paralytic poliomyelitis occurred in children who had been vaccinated. Fortunately, both were mild cases, and all the available evidence indicates that the vaccine was given during the incubation period of the disease. The cases occurred in widely different parts of the country—London and Derbyshire. The other is that it is going to be possible to vaccinate only about 200,000 children instead of the 300,000 to 500,000 originally planned. In May sufficient vaccine was issued to vaccinate 200,000 children. The Ministry has now announced that the safety tests successfully passed by all previous batches cannot be completed on any further batch in time to enable local authorities to arrange for the inoculation of more children by the end of June, the closing date for the vaccination campaign.

Fortifying Flour

The announcement of the Government's acceptance (reported in this Correspondence last month) of its expert panel's advice that there is no ascertainable difference dietetically between National Flour of 80% extraction and 70% extracted flour enriched by the addition of aneurine, nicotinic acid and iron, has provoked strong protests from both *The Lancet* and the *British Medical Journal*. Both journals publish the memorandum of a conference appointed by the Medical Research Council to prepare evidence for submission to the Government panel, and this shows that the panel's decision was opposed to the advice of the Medical Research Council conference. In addition, according to *The Lancet*, the Government's decision is also against the advice of their own medical advisers. In the opinion of the Medical Research Council, the consumption of a 70% extraction flour, even if partially fortified, "constitutes a risk which can be avoided". *The Lancet*, in a leader reminiscent of the days when Thomas Wakley occupied the editorial chair, comments that "the national policy of high extraction—adopted on grounds of economy and health—is to be replaced by a weaker policy of fortification. The millers have virtually settled the matter for themselves—though it must be pleasant for them to have the Government's approval. . . . As things stand there is every prospect of the nation returning to the familiar situation in which people receive what it suits the millers to give them."

Fluoridation of Water

As the time approaches for the initiation of the experiment of fluoridating the water supply in four areas—Anglesey, Andover, Kilmarnock and Watford—in order that the effect upon dental caries may be studied and compared with the findings in four comparable areas in which the water supply has not been fluoridated, the small minority opposed to the experiment is becoming increasingly vocal. So much so that the Government has felt compelled to refer the matter back to the Medical Research Council for a further opinion. The main allegation against fluoridation is that it might have harmful effects on the health of those drinking the water. The Council has now informed the Ministry that in the view of its experts there is no evidence warranting alteration or abandonment of the fluoridation projects now envisaged. The experts agree in general with the conclusions of the United Kingdom Mission to the United States to investigate the matter there in 1953, that there is no definite evidence that the continued consumption of fluorides in water at a level of about 1 p.p.m. in drinking water is in any way harmful to health, and they consider that if any untoward effect is revealed by future research this is most unlikely to be serious.

London, July 1956. William A. R. Thomson

ABSTRACTS *from current literature*

MEDICINE

Respiratory Insufficiency and Chronic Cor Pulmonale.

I. Mack and G. L. Snider: *Circulation*, 13: 419, 1956.

Because of newer techniques of treatment, a small but ever-increasing number of patients with chronic pulmonary disease are surviving long enough to develop chronic cor pulmonale. An attempt has been made to correlate the newer knowledge of aberrations of cardiocirculatory and respiratory physiology in chronic pulmonary disease.

Respiratory insufficiency may be due in varying proportions to: (1) ventilatory dysfunction or impairment of the ability to move air into or out of the lungs; this may be of two types: (a) obstructive, due primarily to airway narrowing and (b) restrictive, due to disordered function of the thoracic bellows or diminished pulmonary distensibility; (2) unequal distribution of inspired air to the alveoli (intrapulmonary mixing); (3) uneven perfusion or distribution of capillary blood flow; (4) impaired diffusion or transfer of oxygen across the alveolar capillary barrier; (5) impaired cleansing of the lung.

The same abnormal physiological change may result from pathological conditions which differ widely in etiology; furthermore, a particular disease may give rise to widely differing functional patterns.

The types of pulmonary disease causing chronic cor pulmonale may be divided into two main categories: (1) Type I, pulmonary diseases associated with chronic diffuse obstructive emphysema; (2) Type II, pulmonary diseases in which the pathological process tends to be localized in or about the pulmonary vessels. In some instances, a case belongs mainly in one category but may demonstrate some features of the other.

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The strain on the right ventricle is a result of: (1) increased resistance to pulmonary blood flow and (2) increased cardiac output (when present). Increased resistance to pulmonary flow may be due to: (a) reduction in calibre and distensibility of the pulmonary vascular bed which may be structural or related to hypoxia; (b) polycythæmia and (c) intrapulmonary vascular shunts.

Respiratory insufficiency may be suspected from the history. Physical and roentgenological examinations may be confirmatory, but pulmonary function tests are necessary for a precise evaluation of the functional abnormalities. The recording of a physiological, as well as a pathological diagnosis is a useful practice in the individual case.

The presence of right ventricular enlargement can only be detected clinically when the chronic cor pulmonale is moderately advanced. However, clinical and roentgenological evidence of pulmonary hypertension in chronic pulmonary disease indicates that right ventricular hypertrophy is probably present. The electrocardiogram may be helpful even in the absence of a definite strain pattern in the right heart since the electric position of the heart is often suggestive. Cardiac catheterization provides the best method for the early detection of pulmonary hypertension.

The treatment of chronic cor pulmonale is much more hopeful today than in the past. It is most satisfactory when cor pulmonale is due to pulmonary disease of Type I. Intensive therapy of the bronchopulmonary disease is as important as specific cardiac measures. The objectives of therapy are to combat infection, produce an adequate airway and improve effective alveolar ventilation. This may partially reverse many of the pathological changes in the lung responsible for hypoxia and the anatomical reduction in the pulmonary vascular bed. Bronchodilators, breathing exercises, sputum liquefiers, Diamox, corticosteroids and cardiac therapy are all important. S. J. SHANE

Induced Azotemia in Humans Following Massive Protein and Blood Ingestion and the Mechanism of Azotemia in Gastrointestinal Hemorrhage.

T. D. COHN *et al.*: *Am. J. M. Sc.*, 231: 394, 1956.

In healthy adult males, a single feeding of a large quantity of whole blood produces a small rise in the blood urea nitrogen level. The peak rise occurs early, within 12 hours. Single equivalent protein feeding of beefsteak or protein concentrate, or both, to the same subjects produces a large rise in blood urea nitrogen. The peak rise also occurs early, within 12 hours. In both instances the azotæmia appears to be dependent upon the degree of absorption and metabolism of the ingested proteins. The protein of whole blood is not absorbed as readily as beefsteak or protein concentrate.

The quantitative 24-hour urinary nitrogen excretion is directly proportional to the degree of absorption and metabolism of the ingested protein. This value is much lower for ingested blood than for other proteins.

The important factors in the azotæmia of gastrointestinal hæmorrhage are: (a) The size of the hæmorrhage: after venesection and ingestion of a critical amount of whole blood, a significant rise in the blood urea nitrogen develops and a marked fall in urea clearance occurs. The peak rise depends upon exceeding the critical level for blood loss, thus producing a contracted blood volume with diminution in renal excretory function. (b) Pre-existing renal disease: this will be aggravated by an even smaller compromise of the circulation and may cause the peak blood urea nitrogen level to rise earlier (within 12 hours). (c) Protein feeding: this may serve as a large source for early elevation of the blood urea nitrogen. If the renal excretory function is impaired, the absorption of ingested protein food from the gastrointestinal tract will contribute greatly to the azotæmia. S. J. SHANE

Exfoliative Gastric Cytology.

L. VAN DER REIS, J. A. RIDER AND J. K. FROST: *Am. J. M. Sc.*, 231: 249, 1956.

Routine exfoliative cytological investigation is again shown to be of definite value as an aid to diagnosis of gastric malignancies. In a series of 70 patients with symptoms of upper gastrointestinal disease, 8 were proved histologically to have a malignancy of the stomach. By exfoliative cytology, 6 of these were detected. Four were definitely diagnosed as "positive" for malignant cells. Results can be improved by utilizing certain refinements in cytological technique discussed in the paper.

When an unequivocal cytological diagnosis of malignancy was rendered, the accuracy in this study was 100%. When cells were present which were felt to be diagnostically inconclusive, 25% of the patients proved to harbour a cancer. When a negative report was rendered, 3% had carcinoma. S. J. SHANE

Albuminuria in Congestive Heart Failure.

G. A. RACE, C. H. SCHEIFLEY AND J. E. EDWARDS: *Circulation*, 13: 329, 1956.

Albuminuria may be an integral part of the picture of congestive heart failure. Of 161 patients in whom the histological renal findings were considered to be either normal or to be of such a nature as not to be responsible in themselves for albuminuria and in whom clinically obvious causes for albuminuria had been eliminated (group 1 of this study), 141 or 88% had albuminuria.

The incidence of albuminuria was about equal among the various types of heart disease when heart failure existed. A trend existed for the grade of albuminuria to parallel the grade of heart failure.

Based on a study of 21 patients, there seemed to be a correlation between the grade of albuminuria and the group of hypertension, according to funduscopic examination. No correlation was found between the grade of albuminuria on one hand and the systolic or diastolic values for blood pressure, the known duration of elevated blood pressure, the grades of hæmaturia or the values for blood urea on the other.

Among the 161 patients with heart failure in their group 1, there was no predominant renal lesion associated with any one cardiac lesion. S. J. SHANE

The Relationship Between Hypertension and Coronary Occlusion.

F. GOLDSTEIN *et al.*: *Ann. Int. Med.*, 44: 446, 1956.

After many years of intensive experimental and clinical research on hypertension all over the world, there is still no agreement as to the causes and effects of hypertension or as to the indications for treatment. Until recently it had been generally accepted that hypertension is an important predisposing factor in the pathogenesis of coronary occlusion. Recent changes in generally accepted criteria of hypertension have, however, led to the conclusion that "hypertension, if it is a factor at all, is not the all-important one in men who sustain coronary occlusion", but that "hypertension is a very significant factor in women who sustain coronary occlusion."

These conclusions were based chiefly on the finding that more than 70% of 500 men who sustained coronary occlusion were previously normotensive. Among 100 women with coronary occlusion, 71% were hypertensive and only 29% were normotensive. The question whether hypertension is causally related to coronary occlusion and myocardial infarction as well as to a number of other cardiovascular complications is a crucial question, since on its answer depends to a large extent the clinician's decision as to treatment.

In the present analysis, the data presented by previous workers are used and added to similar data obtained

from the autopsy records of the Pennsylvania Hospital for the years 1947-1954.

The last consecutive 200 cases since 1947 with myocardial infarction on postmortem examination were analyzed. The highest repeated and sustained blood pressure was recorded in each instance.

The total number of cases analyzed was 1,960, consisting of 1,581 males and 379 females. Of the males with coronary occlusion, 23.7% had hypertension as defined by modern criteria; of the 379 women 57.0% had associated hypertension.

It would appear, therefore, that hypertension in both sexes is *one* of several factors involved in atherogenesis, atherosclerosis and the causation of coronary occlusion and myocardial infarction. Other factors in these processes presumably are diabetes mellitus, certain disturbances in lipid metabolism and the sex hormone. It would appear that up to the menopause women enjoy a fair degree of protection from atherosclerosis, but that after the menopause the number of coronary occlusions associated with, and presumably causally related to, hypertension approaches and eventually equals the number observed in men of similar age. Therefore, the hypertensive factor is presumed to be of equal absolute importance in both sexes, but because in the male other factors operate additionally to accelerate atherogenesis and to cause coronary occlusions, hypertension is of relatively less importance in the male. The positive correlation between hypertension and the incidence of coronary occlusion should be considered, among other factors, in deciding whether a patient with hypertension should receive antihypertensive therapy. S. J. SHANE

SURGERY

Peptic Ulcer of the Second Part of the Duodenum.

C. W. CLARK: *Ann. Surg.*, 143: 276, 1956.

Ulcer more than 5 cm. beyond the pylorus is more common than reported. The symptoms are pain resembling gallstone colic perhaps unrelated to food, perhaps not relieved by antacids. Severe hæmorrhage is common. The lesion is often missed by the radiologist. Roscoe Graham coined the term "duodenal ulcer occulta", for the surgeon may also miss it. Four examples are cited.

BURNS PLEWES

Surgical Treatment of Aortic Stenosis.

C. P. BAILEY *et al.*: *J. Thoracic Surg.*, 31: 375, 1956.

Severe rheumatic aortic stenosis is a medically intractable and often a promptly fatal illness. However, some patients may survive for years, although with increasing incapacitation. This lesion is reasonably responsive to appropriate surgical separation of the obliterated commissures. This should be performed, whenever feasible, by the transaortic route, using digital "vision" to explore the valve and to control the course of any instrumentation. Splitting of one or more fused commissures by simple finger pressure is possible in almost one-half of the patients. Instrumental aid is mandatory in the rest.

Coexisting mitral and tricuspid stenosis may be approached and relieved satisfactorily from the right side through the same right anterior thoracic incision. Indeed, it is now our custom to perform elective surgery for "isolated" mitral stenosis by the right-sided thoracic approach largely in order that any other valvular conditions unexpectedly encountered may be treated simultaneously. The operative mortality and the clinical improvement obtained in surgery for aortic stenosis now closely approach the satisfactory levels established in commissurotomy for mitral stenosis.

Pertinent pathological and physiological abnormalities observed in aortic stenosis are presented. Concepts and techniques of surgery for its alleviation are detailed, together with management of patients.

The improved techniques of management of isolated aortic stenosis and of combined mitral and aortic stenosis are illustrated. Results of the authors' experience are summarized.

Trivalvular (mitral, aortic, tricuspid) exploration is recommended by way of a right-sided (third or fourth anterior intercostal space) incision whenever possible in all patients operated upon for a single rheumatic stenotic valve lesion. All correctable lesions found should be treated at the same operative session. S. J. SHANE

Re-opening the Case of the Abdominal Aortic Aneurysm.

I. S. WRIGHT, E. URDANETA AND B. WRIGHT: *Circulation*, 13: 754, 1956.

Technical advances in the surgical treatment of abdominal aortic aneurysm justify further examination of this treatment.

The great majority of abdominal aortic aneurysms are arteriosclerotic; syphilitic and mycotic aneurysms are now very rare. The life expectancy is poor, 85 to 95% of patients dying within five years of the diagnosis. This type of aneurysm should be regarded as seriously as cancer. The symptoms and signs are varied and often masked by other pathological processes but their careful analysis frequently leads to the correct diagnosis. Roentgenographic studies, both with standard techniques and visualization with contrast media, are usually helpful in confirming the diagnosis. Each case should be analyzed in terms of suitability for surgery; the great majority can be successfully operated upon. Various types of surgical approach have been tried, but today the emphasis is on resection of the aneurysm and its replacement by a graft. Homologous aortic grafts are more widely used at present, but plastic grafts of nylon, orlon, and vinyon are being tried and will possibly be used in the majority of cases in the future. The indications, reasons for caution and contraindications have been analyzed. Rupture of an abdominal aneurysm is the most common fatal complication, but with modern technique and prompt action, an increasing number of these cases are being successfully operated upon.

The technical advances of surgery have greatly improved the outlook for the treatment of the aneurysm itself, but it must be borne in mind that most of these patients are over 60 years of age and have widespread vascular disease or other malignant disease from which more than 50% die within five years. S. J. SHANE

Imperforate Anus with Agenesis of the Vagina.

B. D. COHN AND D. R. MURPHY: *Ann. Surg.*, 143: 430, 1956.

A case is reported from the Montreal Children's Hospital of a 7-year-old child with incontinence of urine and fæces since birth, having no vagina, an imperforate anus and a recto-perineal fistula. After cystoscopy and pyelograms showed a normal urinary tract and skin and ovarian biopsies showed the patient to be a chromosomal female with normal ovarian tissue, an abdomino-perineal dissection was done, the bowel distal to the levators closed to remain as a vagina and the recto-sigmoid pulled through the dissected anal sphincter. She became continent as to both urine and fæces.

This appears to be the first successful reconstruction for this rare combination of anomalies. BURNS PLEWES

Nasopharyngeal Carcinoma: An Account of the Cranial Nerve Lesions Found in 185 Cases.

M. LAWLEY: *Australia & New Zealand J. Surg.*, 25: 170, 1956.

Out of 185 cases of nasopharyngeal carcinoma in Malaya, 48% showed cranial nerve damage. The abducens and trigeminal nerves were most frequently involved. Two main groups of lesions are described: (a) the second, third, fourth, fifth and sixth nerves are involved; (b) there is a lesion of one or more of the last four cranial nerves and of the cervical sympathetic chain.

BURNS PLEWES

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OBSTETRICS AND GYNÆCOLOGY

Congenital Abnormalities of the Uterus and Pregnancy.

J. A. HOLMES: *Brit. M. J.*, 1: 1144, 1956.

Nine cases of pregnancy associated with congenital uterine abnormality are reported and a simple working classification is suggested. The incidence of the condition is probably 1 in 1,000 pregnancies. It is often associated with other congenital abnormalities, particularly of the urinary tract. For this reason a full urinary investigation should be done in all cases.

In types A, B and D there is little extra risk to mother or fetus. In types C, E and F the maternal and fetal risks are maximal, owing to the increased incidence of abortion, malpresentation and manipulations during labour. The ante-partum complications and the complications occurring during labour are mentioned.

The place of elective Cæsarean section is discussed. It is suggested that its use be governed by the type of abnormality present; only in types C, E and F should elective Cæsarean section be considered.

ROSS MITCHELL

RADIOLOGY

A Report on Hypaque, A New Intravenous Urographic Medium.

M. E. SPEICHER: *Am. J. Roentgenol.*, 75: 865, 1956.

This report is based on 800 consecutive intravenous urographies at Squier Urological Clinic in which Hypaque was employed as the contrast medium. Preliminary skin testing for sensitivity proved of little practical value; a history of allergy was much more valuable in indicating possible reactions, none of which were serious. Side-effects were noted in 10.4%, all minor and transitory; 85% of the urograms were diagnostically satisfactory. Only one of 10 patients known to be hypersensitive to other contemporary urographic agents showed undesirable side-effects with Hypaque.

This experience leads the author to the conclusion that Hypaque is a very satisfactory agent for intravenous urography, with minimal reactions, and a safe medium to use in patients who have reacted to other intravenous urographic agents.

NORMAN S. SKINNER

Intravenous Urography; A Comparative Study of Neo-iopax and Urokon.

A. S. TUCKER AND G. DI BAGNO: *Am. J. Roentgenol.*, 75: 855, 1956.

At the Cleveland Clinic, during the period April to September 1953, Urokon (25 c.c. of 30% solution) and Neo-iopax (20 c.c. of 50% solution) were used alternately in routine urograms on 2,000 patients. The results were very carefully studied. Neo-iopax caused minor reactions in 55.2%, Urokon in 45.3%. Local reactions were more common with Neo-iopax, while systemic reactions occurred oftener with Urokon. No serious reaction was encountered. Preliminary testing for sensitivity was rarely employed. Urokon was slightly superior to Neo-iopax in demonstrating renal function and was significantly better in regard to density of urograms.

NORMAN S. SKINNER

Roentgenographic Behaviour of the Ureter.

H. B. FRISCHKORN, JR.: *Am. J. Roentgenol.*, 75: 877, 1956.

Multiple or serial radiographic exposures can demonstrate peristaltic activity in the renal calices and pelvis and in the ureter. The normal functioning ureter is in constant movement and can be expected to empty the upper urinary tract in seven to ten minutes when filling has been by the retrograde method. Such emptying constitutes the most accurate radiographic criterion of ureteral function. Drugs and anæsthesia do not affect ureteral function directly but only as they affect diuresis. Local infection increases ureteral activity. Obstruction at first increases ureteral activity, to be followed later by atony.

The normal ureter is an autonomous organ capable of normal function even when deprived of its nerve supply. The only stimulus necessary for normal ureteral peristalsis is the stretching of its muscle fibres. Antiperistalsis probably never occurs in the normal ureter, and regurgitation of urine from the bladder back into the ureter is probably always abnormal. Transected ureters anastomosed to the intestine or bladder show normal activity, in the absence of stricture or infection.

NORMAN S. SKINNER

DERMATOLOGY

Leukoplakia Buccalis and Oral Epithelial Nævi: A Clinical and Histological Study.

B. E. D. COOKE: *Brit. J. Dermat.*, 68: 151, 1956.

The author describes the historical background of the term leukoplakia. He finds that all white thickened patches in the mouth are called leukoplakia and given the same symptoms, histopathology and prognosis.

Thirty-six cases of leukoplakia buccalis were studied clinically and histologically. This condition is divided into four clinical groups: (1) Smoker's keratoses occurred on the palate and tongue in pipe smokers and on the cheeks in cigarette smokers. Mucous glands of the palate develop a characteristic hypertrophy in pipe smokers. The lip (either upper or lower) was involved in 5 of 12 cases. (2) Frictional keratoses occurred in 18 patients. Their location depended on the site of friction from teeth or dentures; the most common one was on the cheeks along the interocclusal line. (3) Three cases of leukoplakia associated with tertiary syphilis were present in this series. (4) Idiopathic keratoses were diffuse and located on tongue or cheeks. Two cases fitted into this category.

Six cases of oral epithelial nævi were described. They occurred at any age, were symmetrical and were most frequent at the lingual sulcus. Differential points between epithelial nævi and leukoplakia are fully discussed. Also covered in this article is the differential diagnosis between leukoplakia and lichen planus, and the details of a technique for biopsy of the oral mucosa. This paper has numerous excellent photographs and photomicrographs. Anyone having an interest in leukoplakia should read it in its entirety.

ROBERT JACKSON

THERAPEUTICS

Pyrazinamide: Comparison with Isoniazid-Para-Aminosalicylic Acid in Active Pulmonary Tuberculosis.

S. PHILLIPS AND G. E. HORTON: *Am. Rev. Tuberc.*, 73: 704, 1956.

Previous studies with pyrazinamide in pulmonary tuberculosis have led several groups of investigators to the conclusion that, although pyrazinamide-isoniazid is the most powerful of the available tuberculosis chemotherapies, it should not be routinely used in pulmonary tuberculosis because of the hepatotoxicity of pyrazinamide. This serious view of the toxicity of pyrazinamide was not completely accepted by all investigators, and the question arose whether results obtainable with pyrazinamide-isoniazid were so markedly superior as to justify toleration of a certain relatively low incidence of hepatotoxicity. In an attempt to answer this question, a randomized study was begun at the Veterans Administration Medical Teaching Group Hospital in which pyrazinamide-isoniazid was compared in efficacy and toxicity with isoniazid-para-aminosalicylic acid. This study included 93 patients with active pulmonary tuberculosis, 38 of whom were treated with pyrazinamide-isoniazid for a minimum period of 4 months, and compared with 55 patients treated similarly with isoniazid-PAS.

The pyrazinamide-isoniazid regimen may have been slightly superior because of a somewhat lesser need for additional measures, such as collapse or resectional therapy, and a somewhat more prompt disappearance of tubercle bacilli from the sputum.

There were 2 instances of complicating jaundice and 3 other cases of hepatitis among the 38 patients on pyrazinamide-isoniazid. No serious toxicity complicated the treatment with isoniazid-PAS, although one patient could not tolerate PAS for longer than one year.

Not a single patient treated with pyrazinamide-isoniazid excreted tubercle bacilli in the sputum resistant to isoniazid. One patient treated with isoniazid-PAS showed isoniazid-resistant organisms in one sputum specimen just prior to reversal of infectiousness.

The bromsulphalein dye retention test was found to be the most useful in detecting early evidence of hepatotoxicity. The cephalin flocculation did not become significantly abnormal in any of the patients in the present study.

It is believed that the incidence and severity of the hepatitis, which may complicate treatment with pyrazinamide-isoniazid, is probably too high a price to pay for the slight therapeutic superiority which may be obtained. Accordingly, the writers concur in the belief, expressed initially by others, that this regimen should not be used in routine forms of tuberculosis when other suitable agents are available. S. J. SHANE

Simplified Heparin Therapy of Impending and Acute Myocardial Infarction.

H. ENGELBERG: *Ann. Int. Med.*, 44: 466, 1956.

The administration is described of concentrated aqueous heparin subcutaneously for the initial one to two weeks in a group of 19 coronary atherosclerotic patients with an impending myocardial infarction.

The results in this series were good: two patients developed an acute transmural infarction, a diagnosis of subendocardial infarction was made in four, and in the other 13 apparently no infarction took place during therapy. Four of these 13 discontinued therapy prematurely, and in three, acute infarction or death occurred within several months.

Many other actions of heparin are reviewed which indicate its superiority over other anticoagulants in the therapy of impending and acute myocardial infarction.

In 15 patients with an acute myocardial infarction, continuous anticoagulation has been maintained for the first three weeks, with concentrated aqueous heparin administered subcutaneously every 12 or every 24 hours. This method is simple and economically feasible, and requires few laboratory tests for control.

Reasons are presented indicating that arguments against the routine use of anticoagulants in all cases of myocardial infarction do not apply to heparin.

S. J. SHANE

Cardiovascular Effects of Sodium Lactate: Effect in Normal Subjects and in Various Arrhythmias.

S. BELLET, F. WASSERMAN, AND J. I. BRODY: *Am. J. M. Sc.*, 231: 274, 1956.

The cardiovascular effects of infusion of molar sodium lactate in the presence of various arrhythmias are compared with those observed in the normal heart. These manifestations were studied in a total of 32 patients. Included were normal subjects, patients with various types of myocardial abnormalities with normal sinus rhythm, partial A-V heart block, sinus bradycardia, carotid sinus hypersensitivity, extrasystoles and QRS widening, associated with various etiological factors (partial and complete A-V heart block and the idioventricular beats of cardiac arrest). In most subjects, the dose administered ranged from 100 to 200 ml. given in 10 to 15 minutes. The electrocardiographic changes were correlated with the blood pH, CO_2 combining power, lactic acid and the following electrolytes—sodium, potassium and calcium.

Electrocardiographic alterations were observed chiefly in subjects with slow heart rates occurring with sinus bradycardia and partial and complete A-V heart block. Most of these patients showed evidence of an increase in the heart rate at the height of the sodium lactate effect; the maximum changes were usually observed at or within a few minutes after completion of the infusion. The occasional T wave and ST segment changes observed are believed to be the result of electrolyte alterations in the heart following infusion of sodium lactate.

This solution is fairly well tolerated and relatively few toxic manifestations were observed. In three subjects with advanced heart disease, transient extrasystoles were observed following the infusion. Extrasystoles present in another patient without evidence of organic heart disease were abolished following lactate administration.

There was no alteration in the degree of carotid sinus hypersensitivity in four subjects after infusion of molar lactate.

The molar sodium lactate showed a definite tendency to narrow widened QRS complexes associated with partial and complete A-V heart block, bundle branch block and the idioventricular beats of cardiac arrest.

The mechanism of the clinical and electrocardiographic effects is discussed and their clinical significance is outlined.

The authors' impression at this time is that the effects observed can best be explained by the production of alkalosis and the effect of the lactate. S. J. SHANE

Treatment of Human Pulmonary Tuberculosis with Cycloserine.

I. G. EPSTEIN, K. G. S. NAIR AND L. J. BOYD: *Dis. Chest*, 29: 241, 1956.

Cycloserine, a new antibiotic, has been used in the treatment of 57 cases of pulmonary tuberculosis. These include 37 original cases previously reported and 20 additional subjects. Twenty-five were acute cases, previously untreated; 32 were chronic cases, therapeutically resistant to prior antimicrobial therapy.

Cycloserine was administered orally in a dose of 20 to 25 mg./kg. of body weight per day (1.0 and 1.5 g.), in divided doses.

The incidence of side-reactions was low. On the basis of neurological symptoms, both excitatory and depressant, it was necessary to discontinue therapy on five patients. Skin rashes of short duration and unknown cause occurred in three, in all of whom cycloserine was continued without further difficulty.

Although this study has run for a comparatively short time (5 to 40 weeks), the following conclusions may be drawn from the data at hand: Cycloserine has been found to be an efficient antibiotic agent in the treatment of acute, previously untreated cases of pulmonary tuberculosis. Sputum conversion, x-ray film clearing, gain in weight, and reduction of fever occurred promptly. It fills the need for an antimicrobial agent in those cases of chronic tuberculosis which have failed to respond to existing drugs, especially patients who are inoperable because of extent of disease or poor condition.

In the daily dose of 20 to 25 mg./kg. of body weight, over periods of up to 10 months of continuous therapy, cycloserine elicited few reactions other than those in psychotics and epileptics. The milder untoward symptoms disappear upon continued therapy.

Resistance to cycloserine by the tubercle bacillus has not developed either clinically or in *in vitro* studies, in contrast to currently available antituberculosis drugs.

Studies are being carried out to determine the therapeutic compatibility between cycloserine and streptomycin, or isoniazid. There may result a mixture between these which will prevent resistance and diminish or abolish toxicity. S. J. SHANE

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OBITUARIES

DR. CHARLES J. McCABE, 65, chairman of the Hamilton, Ont. Board of Health, died in St. Joseph's Hospital, Hamilton, on June 10. Dr. McCabe was born in Hamilton and graduated from the University of Toronto, afterwards doing postgraduate work in New York. He was an assistant coroner, and in 1947 was appointed chief medical examiner for the Civil Service Commission in the Hamilton district.

He is survived by his widow, a son and a daughter.

DR. FARQUHAR MacLENNAN, 85, who was the oldest practising physician in Windsor, Ont., until his retirement last year, died at Grace Hospital, Windsor, on June 21. He had been medical superintendent of Grace Hospital from 1924 to 1955. Dr. MacLennan was born at Lochalsh, Bruce County, Ont. He graduated from Trinity College—now part of the University of Toronto—in 1895 and began practice at Kintail. In 1901 he went to Ripley, where he practised until 1913, at which time he moved to Windsor. He was the second president of the Essex County Medical Society, and in 1947 was made an honorary life member of the Ontario Medical Association. He served on the school of nursing committee of Grace Hospital as well as on the hospital management board.

Dr. MacLennan is survived by his widow, a son and a daughter.

DR. VINCENT K. O'GORMAN, 67, a general practitioner at Edmonton, Alta., died on June 14. He was born at Renfrew, Ont., and graduated from the University of Toronto in 1915. During World War I he served with the British Army in India, Iraq, France and England. He practised at Sudbury and Timmins, Ont., before going to Edmonton in 1929.

Dr. O'Gorman is survived by four brothers and a sister.

DR. WINDSOR TRUAX, 76, a general practitioner for over 40 years in the Boundary district of British Columbia, died at Vancouver on June 30. Dr. Truax was born at Farnham, Que., and graduated from McGill University in 1903. In 1904 he began practice at Ladysmith, V.I., and later settled at Grand Forks. He retired in 1947. Dr. Truax was a life member of the College of Physicians and Surgeons of British Columbia.

He is survived by his widow, a daughter and a son.

DR. CHARLES A. WHITTY, a surgeon at Norwichtown, Conn., died at New Haven, Conn., on June 18. He was born in Toronto and graduated from Queen's University, Kingston, Ont., in 1929. He then moved to Norwichtown where he became assistant chief surgeon of the State of Connecticut. He was a Fellow of the American College of Surgeons.

Dr. Whitty is survived by his widow and a son.

FORTHCOMING MEETINGS

CANADA

INDUSTRIAL SECTION, ONTARIO MEDICAL ASSOCIATION, AND INDUSTRIAL MEDICAL ASSOCIATION OF THE PROVINCE OF QUEBEC, Combined Annual Meeting, Hamilton, Ontario. (Dr. Glenn Sawyer, Executive Secretary, Ontario Medical Association, 244 St. George Street, Toronto, Ont.) September 26-28, 1956.

UNITED STATES

INTERNATIONAL CONGRESS OF HEMATOLOGY, Boston, Massachusetts. (International Society of Hematology, New England Center Hospital, Harrison Avenue at Bennett Street, Boston 11, Mass.) August 26-September 1, 1956.

SIXTH INTERNATIONAL CONGRESS OF BLOOD TRANSFUSION, Boston, Massachusetts. (Professor I. S. Ravdin, President, New England Medical Center, Harrison Avenue, Boston 11, Mass.) August 29-September 2, 1956.

FIRST INTER-AMERICAN CONFERENCE ON OCCUPATIONAL MEDICINE AND TOXICOLOGY, Miami, Florida. (Dr. Homer F. Marsh, Dean of the School of Medicine, University of Miami, Fla.) September 3-7, 1956.

INTERNATIONAL COLLEGE OF SURGEONS, 10th International Congress, Chicago, Illinois. (Dr. Max Thorek, 1516 Lake Shore Drive, Chicago, Ill.) September 9-13, 1956.

INTERNATIONAL CONGRESS OF CLINICAL CHEMISTRY, New York, N.Y. (Mr. J. C. Reinhold, 711 Maloney Building, Hospital of the University of Pennsylvania, Philadelphia 4, Pa.) September 9-14, 1956.

OTHER COUNTRIES

WORLD FEDERATION FOR MENTAL HEALTH, Ninth Annual Meeting, Berlin, West Germany. (The Secretary, W.F.M.H., 19 Manchester Street, London, W. 1, England.) August 12-18, 1956.

FOURTH INTERNATIONAL CONGRESS ON DISEASES OF THE CHEST, Cologne, West Germany. (Dr. Murray Kornfeld, American College of Chest Physicians, 112 Chestnut Street, Chicago 11, Ill.) August 19-23, 1956.

SECOND INTERNATIONAL CONGRESS OF PHYSICAL MEDICINE, Copenhagen, Denmark. (Dr. B. Strandberg, Koebnhavns Amts Sygehus i Gentofte, Hellerup, Denmark.) August 20-24, 1956.

SECOND INTERNATIONAL CONGRESS OF DIETETICS, Rome, Italy. (Dr. Margaret A. Ohlson, The American Dietetic Association, 620 North Michigan Avenue, Chicago 11, Ill.) September 10-14, 1956.

EUROPEAN SOCIETY OF CARDIOLOGY, Second Congress, Stockholm, Sweden. (Professor K. E. Grewin, Södersjukhuset, Stockholm.) September 10-14, 1956.

25TH INTERNATIONAL CONGRESS AGAINST ALCOHOLISM, Istanbul, Turkey. (Bureau International contre l'Alcoolisme, Case Gare 49, Lausanne, Switzerland.) September 10-15, 1956.

SEVENTH INTERNATIONAL CONGRESS OF CATHOLIC DOCTORS, The Hague, The Netherlands. (Dr. Weebers, Nijmegen, Holland.) September 10-16, 1956.

SIXTH INTERNATIONAL CONGRESS OF HYDATID DISEASES, Athens, Greece. (Professor B. Kourias, Croix-Rouge Hellenique, 1 rue Mackenzie King, Athens.) September 14-16, 1956.

FOURTH INTERNATIONAL CONGRESS OF INTERNAL MEDICINE, Madrid, Spain. (Sociedad Espanola de Medicina Interna, Montalera 90, Madrid.) September 19-23, 1956.

MEDICAL WOMEN'S INTERNATIONAL ASSOCIATION, Extraordinary General Meeting, Bürgenstock, Switzerland. (Dr. Janet Aitken, 30a Acacia Road, London, N.W. 8, England.) September 21-23, 1956.

THIRD EUROPEAN CONGRESS OF ALLERGOLOGY, Florence, Italy. (General Secretary, Professor Umberto Serafini, Istituto di Patologia Medica, Viale Morgagni, Florence.) September 26-29, 1956.

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PROVINCIAL NEWS

BRITISH COLUMBIA

Dr. Margaret A. Kennard, associate professor in neurology in the Medical Faculty of the University of British Columbia, was elected to the Council of the American Electro-Encephalographic Association at its recent meetings at Atlantic City.

Dr. E. W. Wylde of New Westminster has been elected president of the St. John's Ambulance Council of that city. Also elected as corps surgeon is Dr. R. Harper.

Dr. David Steele of Vancouver was elected president of the Canadian Foundation for Poliomyelitis at the annual meeting of that body, held in the Hotel Vancouver. He succeeds L. D. Currie of Halifax. Dr. Steele is Chairman of the Medical Advisory Board of the B.C. Polio Fund.

Dr. E. G. Dower of the University of British Columbia staff has been granted another fellowship by the Canadian Life Insurance Medical Fellowship Fund to continue his researches into heart disease. This is the third fellowship he has received from this fund.

A new private hospital for chronic and convalescent cases has been opened in Vancouver. This is the Edith Cavell Hospital, and it will help to fill one of the greatest needs of the community. It will accommodate up to 50 patients.

The hospital will be well equipped to give medical care, and can provide oxygen and intravenous therapy where needed. There will be 24-hour nursing supervision. It will have a staff of some 30 people.

The B.C. Hospitals Association recently held a conference of its Women's Auxiliaries Division. One is very apt to forget, or rather not to realize, just how much the devoted and unselfish work of these auxiliaries means to the smooth running of the modern hospital, and how much comfort and good cheer they bring into the lives of the inmates. Only one who has been a hospital inmate, especially away from home, can fully realize what flowers, books, dainty clothing and linen mean to the sick person—and above all how visits and friendly calls help to dispel loneliness. It is the aim of the kindly and generous women of these auxiliaries to provide all these and many other gifts and comforts. Members from hospitals all over the province attended these meetings, and gave details of the magnificent work being done by their hospital auxiliaries.

For instance, Alert Bay has a hospital of six beds—with an auxiliary of six members. This hospital is situated on a small island, just off the northern tip of Vancouver Island, with a small population, largely of Indians. Yet in eight months it raised $808 for its hospital's needs.

Gorge Road, Victoria, has a hospital—the Victoria Nursing Home of former days—and its auxiliary is providing an occupational therapy unit, fully equipped, and will further provide $125 a month to maintain it. Powell River Hospital has an auxiliary which holds a fall fair to raise funds, and visits each patient personally once a week. Prince Rupert Hospital Auxiliary is raising $4,000 for equipment, through sales of a cookbook, reported to be of surpassing excellence. The Penticton General Hospital Auxiliary provides stainless steel containers for the hospital.

Nanaimo, Prince George, Vernon, Trail-Tadanac, Rossland, and many others have similar tales to tell. One could fill many a page with the work these gallant small hospitals are doing, through these auxiliaries. They provide equipment when the hospital is built, and where it is not, they go out and collect the money to build it, as in Surrey, where they have raised $16,000 to date for their new hospital. Other names come to mind—Chemainus, Pender Harbour, Armstrong, Ladysmith. There are 91 of them so far in the Province, and their number grows yearly.

These are the smaller hospitals, and we put them first. The larger hospitals, the Royal Jubilee and St. Joseph's in Victoria, the Royal Columbian and St. Mary's in New Westminster, the Vancouver General Hospital, St. Paul's, Grace, St. Vincent's, Shaughnessy Hospital (as this is written a huge bazaar is in progress in the grounds of this hospital) and so on—these have auxiliaries of varying numbers of members, but every one of them is hard at work. Women of every walk of life, and of every age, are proud and glad to serve on them, and "their work continueth". Or to quote another authority on this sort of woman, one might refer our readers to that marvellous Acrostic on the Virtuous Woman, found at the end of the Book of Proverbs, which seems to the writer of this to describe very well the work of these ladies of the lamp.

. . . She layeth her hands to the distaff
And her hands hold the spindle.
She spreadeth out her hands to the poor
Yea, she reacheth forth her hands to the needy.
. . . . . .
Give her of the fruit of her hands
And let her works praise her in the gates.

J. H. MACDERMOT

MANITOBA

On June 4 the St. James City Council voted in favour of fluoridation. St. James's is the sixth Greater Winnipeg Council to vote in favour, and the combined populations of the six exceed the necessary 85% required by an act of the provincial legislature to permit fluoridation. The general manager of Greater Winnipeg's water supply system states that fluoridated water will be in the mains before November.

The town of Boissevain celebrated its 75th anniversary July 12 to 15. Dr. D. M. McPhail, the town physician, has grown whiskers, as have the other men of the town, and in the historical parade on July 13 he and his black bag rode on an old high bicycle.

Dr. H. P. T. Thorlakson has retired as chief of surgery in the Winnipeg General Hospital. His place will be taken by Dr. C. Burton Stewart, head of the department of urology. Dr. C. W. Clark will be head of general surgery.

Harold H. Lynge, M.D., and Gerd Fischer, M.D., have opened an office at 507 Medical Arts Building, Winnipeg, for the practice of neurosurgery.

N. H. Werner, M.D., is now located at 404 Norlyn Medical Building, Winnipeg, for the practice of ophthalmology.

Dr. Ross McKay Creighton has been appointed director of preventive medicine for Manitoba in succession to Dr. Maxwell Bowman, who died suddenly in April.

Dr. M. H. L. Desmarais has opened an office at 201 Medical Arts Building for the practice of physical medicine and rheumatology.

ROSS MITCHELL

ONTARIO

Among the 26 members of the graduating class of 1906, U. of T., who held a class reunion in Toronto in the third week of June, was Dr. C. W. Slemon who has served as a family doctor for 50 years. Dr. Slemon began by teaching school at Burketon at the age of 18 and subsequently graduated from the University of Toronto in 1906, beginning his practice in Enniskillen, Ont., and moving on in 1920 to Bowmanville, Ont. Two of Dr. Slemon's sons have followed him into the medical profession.

Dr. Harry Cullumbine assumed on July 1 his duties as head of the Pharmacology Department of the University of Toronto. Dr. Cullumbine began his medical career

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in Sheffield and later taught in the Pharmacology Department of the University of Manchester. During the war he served in the R.A.M.C. with the rank of lieutenant-colonel. He later took the chair of physiology and pharmacology in the University of Ceylon, during which time he carried out a number of studies on the physical data of the population. He then returned to England to direct the Medical Research Laboratories of the Ministry of Supply, and while with the Ministry went with a unit to Africa to study nutrition and health problems. As a result he was asked to join the World Health Organization Expert Panel on Nutrition. Dr. Cullumbine has thus had experience not only in pharmacology, including war gases, but also in various fields of physiology, including air pollution and nutrition.

Dr. Elizabeth N. MacKay of the Ontario Department of Health's Division of Medical Statistics, has been given two years' leave of absence from the department to undertake a special temporary appointment in public health statistics in Lima, Peru, under the ægis of the Pan-American Sanitary Bureau of the World Health Organization. Dr. MacKay assumed this appointment on July 1.

From 1951, Dr. MacKay has devoted her full time to work on cancer records and statistics and in this capacity has made an important contribution to the work of the Division of Medical Statistics and the Ontario Cancer Treatment and Research Foundation.

QUEBEC

The highlight of the news from our Division this past month was, of course, the Annual Meeting of the Association in Quebec City. This has been covered elsewhere.

Dr. G. B. Maughan has been appointed professor of obstetrics and gynæcology at McGill University and obstetrician and gynæcologist-in-chief at the Royal Victoria Hospital. He succeeds Dr. N. W. Philpott, who has resigned to enter private practice. Dr. Maughan was born in Toronto and graduated from McGill in 1934. He interned at the Royal Victoria Hospital under Dr. John R. Fraser and eventually was given both university and hospital appointments of increasing responsibilities. He served in the Royal Canadian Navy from 1941 to 1944.

Dr. John C. Locke has been named on a part-time basis as ophthalmologist-in-chief at the Royal Victoria Hospital and professor of ophthalmology and chairman of the department at McGill. He succeeds Dr. Kenneth B. Johnston, who has resigned. Dr. Locke was born in Winnipeg and graduated from McGill. He saw active service with the R.C.A.M.C. from 1943 to 1946.

Queen Elizabeth Hospital in Montreal has opened a campaign for $4,500,000. This is for modernization of existing facilities and the construction of a six-storey addition to the present building. Plans include provision for enlarged additional operating rooms, an extension of x-ray and laboratory space, modernization and extension of the physiotherapy department, and additional facilities for delivery rooms, labour rooms and the nursery. The postoperative recovery room, established at this hospital in 1943, will be enlarged and modernized.

The Montreal Anti-Tuberculosis League recently released its 1955 annual report. In this the medical director of the league, Dr. P. H. Lavergne, reports that 304,574 persons were x-rayed of whom 2,895 showed indications of tuberculosis. Of these, 162 had the disease in a mild form, 187 had moderately advanced tuberculosis, and 45 had tuberculosis in its advanced stage. This is an overall percentage of 9.6, compared with 10.9% for the previous year. The 12 health units operating in surrounding counties of Montreal reported 48 new and 97 old cases of the disease out of a total of 1,263.

Dr. L. P. Belisle, radiologist, reporting on other thoracic diseases which had been indicated in examination of all chest x-rays, said that 1,326 non-tuberculous diseases had been classified. Of these, 1,126 were cardiac conditions, 58 were bronchial diseases and cysts and 76 were benign and malignant tumours. These figures give a clear indication of the good services that the community secures from the work of such a voluntary agency.

The serious financial problems faced by so many of our hospitals were again scrutinized with great care at the three-day annual meeting of the province's 350 Roman Catholic hospitals which was held in Quebec City during the week of June 24. Some 80% of the hospitals were represented and there were as many visitors from outside the province. The Rev. Hector L. Bertrand, president of the Quebec Hospitals Committee, stressed that the establishment of a state health insurance plan may lead to the possibility of state controlled medicine. He felt that the danger can be avoided by frank and loyal exchanges of views between the various organizations concerned.

The all-too-familiar story of costs steadily outstripping revenues was retold by many. For instance, Mr. Paul Tremblay of the Hôtel-Dieu of St. Vallier said that a patient on public assistance in 1952 cost the hospital $11.71 a day. The provincial and municipal contributions toward this cost was $5.50. Today such a patient costs the hospital $14.50, while the contribution from the same sources is $7.50. A loss of $7.00 per day on each one of the large number of such patients being treated in Quebec hospitals leads to the piling up of alarming deficits.

A. H. NEUFELD

CANADIAN ARMED FORCES

Colonel John E. Andrew, E.D., C.D., 46, Senior Consultant to the D.G.M.S. (Army), died suddenly at his home in Ottawa.

Colonel Andrew was born in Prince Edward Island, and graduated from Dalhousie University. He was a Fellow of the Royal Colleges of Surgeons of Edinburgh and Canada, and a member of the editorial board of the Canadian Services Medical Journal.

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During World War II, Colonel Andrew served at Spitzbergen and in Italy and Northwest Europe in field surgical units and hospitals. He also served in Korea and Japan in 1951 as the Commanding Officer and Surgical Specialist of the Canadian Section of the Commonwealth Hospital in Kure. He was appointed to the D.G.M.S. Directorate in 1953.

Colonel Andrew is survived by his widow and daughter.

Brigadier K. A. Hunter, Co-ordinator of Medical Services, Department of National Defence; Surgeon Commodore E. H. Lee, Medical Director General (Navy); Brigadier S. G. U. Shier, Director General Medical Services (Army): and Air Commodore A. A. G. Corbet, Director General Medical Services (Air), along with other selected medical officers of the three medical services attended the annual meeting of the Canadian Medical Association held in Quebec City, June 11-15, 1956.

Each of the Canadian medical services presented papers at the Armed Forces Section. The Navy paper presented by Surgeon Lieutenant Commander D. J. Kidd was entitled, "Medical Aspects of Maritime Arctic Operation". An Army paper on the subject "Medical Services in Cold Weather Warfare" was presented by Major J. E. Gilbert. Squadron Leader L. A. Wright of Air Force Headquarters presented the Air Force paper on "The Medical Aspects of Military Operations by the R.C.A.F. in a Cold Climate".

An outstanding feature of the scientific exhibits was a display arranged by No. 1 Airborne Medical Platoon, R.C.A.M.C., of the special medical equipment used on airborne operations in the Arctic.

Surgeon Commander J. W. Rogers, R.C.N., Principal Medical Officer, H.M.C.S. *Cornwallis*, Cornwallis, N.S., and Surgeon Lieutenant Commander W. C. Wood, R.C.N., who has been serving as Staff Medical Officer on the staff of the Flag Officer Naval Divisions, Hamilton, Ont., have been selected for postgraduate training in medicine beginning July 1, 1956.

Surgeon Commander Rogers, who is certified in Public Health, will continue training in medicine at Toronto; and Surgeon Lieutenant Commander Wood will commence training in Internal Medicine at the Westminster Hospital, London, Ont.

Acting Surgeon Captain H. R. Ruttan, R.C.N., who has completed a two-year appointment as Commandant of the Medical Joint Training Centre, Toronto, has been selected for further postgraduate training in dermatology and will commence training at the University of Toronto upon replacement.

Following a nationwide competition sponsored by the Defence Medical Association, the Ryerson Trophy has been awarded to No. 13 Medical Company, Owen Sound, Ont., commanded by Lt.-Col. A. S. Middlebro, as the most efficient militia medical unit in the Canadian Army. The Shillington Trophy for the second best unit went to No. 24 Medical Company, Vancouver, commanded by Lt.-Col. C. E. Robinson.

Brigadier S. G. U. Shier, D.G.M.S. (Army), recently inspected R.C.A.M.C. installations and arrangements with the 2nd Canadian Infantry Brigade Group in Germany. While in Europe he also visited the Canadian Army Liaison Establishment, London, and Lt.-General A. Drummond, Director General Army Medical Services, British Army.

The National Camp for medical personnel of the Canadian Army (Militia) was held near Camp Borden between July 7-21, 1956. This is only the second time since World War II that this type of training has been conducted. Officers, nursing sisters and men from Militia medical units of all commands attended the camp. The two weeks' training consisted of one week of qualifying courses and one week of tactical exercises and demonstrations.

Major R. C. Elliott, R.C.A.M.C., was promoted Acting Lieutenant-Colonel, July 1, and assumed command of 4 Canadian Field Ambulance, Germany, *vice* Lt.-Colonel J. R. Feindel. The latter replaces Lt.-Colonel B. L. P. Brosseau, R.C.A.M.C. Liaison Officer, Canadian Joint Staff, London, who returns to Canada to take a course in Hospital Administration at the University of Toronto in September.

Major D. H. M. Hall, R.C.A.M.C., was promoted to Acting Lieutenant-Colonel July 1, and commenced a residency in Hospital Administration at Sunnybrook Hospital, D.V.A., Toronto.

Major D. G. Guthrie, R.C.A.M.C., has obtained a diploma in Medical Radiology (Diagnosis), D.M.R.(D), from Queen's University, Kingston, Ont.

Group Captain D. G. M. Nelson, Commanding Officer, Institute of Aviation Medicine, Toronto, has been selected to attend National Defence College, Kingston, Ont., beginning September 1956, at which time Wing Commander J. Powell will assume the duties of Commanding Officer, Institute of Aviation Medicine.

Group Captain G. D. Caldbick was transferred to Air Force Headquarters in July 1956 to the staff of the Director General Medical Services (Air).

Wing Commander R. L. Walsh from the staff of D.G.M.S. (Air) has been transferred to Canadian Joint Staff, London, England, as the R.C.A.F. Medical Liaison Officer.

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BOOK REVIEWS

MEDICAL WRITING. MD International Symposia No. 2. W. C. Alvarez, Former Professor of Medicine, University of Minnesota, Minneapolis; Editor, Modern Medicine, Chicago, Ill., and others. 66 pp. MD Publications, Inc., New York, 1956.

This volume contains contributions to a monograph on medical writing which appeared first in the monthly journal "International Record of Medicine and General Practice Clinics". For anyone who has occasion to write, this symposium can be recommended, for it is full of good things and the contributors are authorities on their subject. The symposium begins with an article by Henry Sigerist, who discusses the physician's writing and reading. He advises beginning the day with the reading of a poem or two, is contemptuous of the newspapers and magazines, and urges that the physician's reading of books be not confined to contemporary literature, but be extended to the classics of the last 5,000 years. Hans Selye of Montreal discusses "How Not to Write a Medical Paper". He is chiefly concerned not with the technique of writing, but with the proper formulation of scientific ideas, and discusses a series of seven traps in the evaluation of scientific data. Dr. Hugh Clegg, editor of the *British Medical Journal*, discusses an editor's prejudices. He emphasizes that the most severe strain on the judicial capacity of an editor is inherent in the selection and rejection of material for publication. He has the usual tilt at the rush for priority in scientific articles and ends with some comments on style and on the meaning of words. Dr. Walter C. Alvarez contributes in his usual dashing style a couple of pages on medical writing. The chief sins he laments are the inability of doctors to stick to the point and to make things simple. The symposium is brought to a conclusion by a long and scholarly essay written by Dr. Felix Marti-Ibánez on books in the physician's life.

MOSBY'S REVIEW OF PRACTICAL NURSING. Edited by Dorothy K. Rapier and others. 322 pp. Illust. The C. V. Mosby Company, St. Louis, Missouri; McAinsh & Co., Ltd., Toronto, 1956. $4.25.

This is a very condensed coverage of the whole field of practical nursing, including basic anatomy and physiology. Written in telegram style, it is designed for rapid review of material already studied. It should be of particular use to practical nurses preparing for examinations and also to older nurses wanting to refer quickly to some forgotten point. The book also contains a section of review questions for answer.

A MANUAL OF FRACTURES AND DISLOCATIONS. B. B. Stimson, Director of Dept. of Bone and Joint Surgery, St. Francis Hospital, Poughkeepsie, New York. 3rd ed. 244 pp. Illust. Lea and Febiger, Philadelphia; The Macmillan Company of Canada Limited, Toronto, 1956. $4.50.

This book is intended as an outline of fracture diagnosis and treatment for medical students, interns, and general practitioners. It would seem to be of particular value to the medical student, giving him an over-all picture of the problems of fracture management, and graphically illustrating with simple line drawings the mechanism of production, the deformity, and the accepted treatment of all the common fractures. For the intern whose interest is drawn to fracture treatment, this book might serve as a portable companion to the larger and more comprehensive Watson-Jones.

The author has been able to complete this review in 224 pages, making the book one that can be read and re-read by the student to memorize the important features of fracture care. He may then proceed to a more extensive study of the problem with a firm foundation of knowledge of the deformity of fractures, and their accepted methods of treatment.

HORMONES IN REPRODUCTION. British Medical Bulletin, Vol. II, No. 2. 170 pp. Illust. Medical Department, The British Council, London, 1955. $2.75.

In his introduction to this symposium, Dr. A. S. Parkes points out that it does not constitute a complete survey of this very wide field, but that each of the contributors has been asked to write on the aspect of the subject which interests him most. As a result there are some omissions and duplications, but the articles are in general of a very high standard. Amoroso and Matthews contribute an article in which the effect of the environment on the breeding cycle in birds and mammals is discussed. It is agreed that although gonadal function is conditioned by a variety of environmental factors, mediation within the organism is not yet satisfactorily understood. Donovan and Harris review neurohumoral mechanisms in reproduction, while Noble and Plunkett of the University of Western Ontario, London, Ont., discuss the biology of the gonadotrophins. There is a further contribution on the chemistry of the gonadotrophins by Morris from the London Hospital. In this he makes a plea for further study of the gonadotrophins, of which only two have been obtained in a satisfactory state of purity, by the more modern methods of fractionation. Articles on the endocrinology of the testis and on the biology of the œstrogens are contributed by Parkes and Zuckerman respectively. There is a striking contribution by Amoroso on the endocrinology of pregnancy, in which he compares certain aspects of this subject in mammals and lower vertebrates. The important role of the placenta in extending and maintaining pregnancy is emphasized. The author points out that while œstrogen and progesterone are necessary for the maintenance of pregnancy in all animals, they may both be supplied from extra-ovarian sources in certain mammals such as man, the monkey and the mare, whereas in others neither of these substances can be supplied in the absence of the ovaries, while in the mouse and rabbit œstrogen but not progesterone may come from an extra-ovarian source. Dr. Callow writes on the biochemistry of the gonadal hormones and Sir Charles Dodds on synthetic œstrogens. Emmens and Venning contribute articles on various aspects of hormone estimations. The latter article is of particular interest to clinicians, since in it the author discusses the diagnostic value of assay of reproductive hormones in establishing the presence of early pregnancy and of hormonal imbalance in a variety of conditions. The endocrinology of mammary growth and function is described by Folley and the roles of the posterior pituitary and the adrenals in reproduction are considered by Cross and Jones. Dr. Swyer concludes his study of hormones and human fertility by stating that in the absence of endocrine infertility factors, the empirical administration of hormones has little or no effect on the promotion of fertility and can only be condemned. As a guide to present-day thinking in the field of reproduction endocrinology, this symposium may be recommended.

ANNUAL EPIDEMIOLOGICAL AND VITAL STATISTICS, 1953. 571 pp. (French and English). World Health Organization, Palais des Nations, Geneva, 1956. $10.00.

The World Health Organization has just published its sixth annual volume of epidemiological, vital and health statistics, a work which contains information relating to the various countries and territories of the world for the year 1953.

In this volume of more than 570 pages, 74 tables give details of the most important aspects of the health situation in all parts of the world—population composition, vital statistics, causes of death, incidence of communicable diseases and their seasonal fluctuations.

Users of this annual series are able to follow, year by year, the progress of hygiene and the evolution of the health situation in various countries. In addition to the subjects for which detailed information is usually given in all the volumes in this series—diseases of childhood, cancer and tuberculosis, for example—the present work contains hitherto unpublished data on mortality from cardiovascular diseases, a topic in which scientific circles are at present taking an ever-increasing interest.

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When the menopause case requires estrogen, prescribe TACE . . . the exclusive oral, fat-stored estrogen released like a natural hormonal secretion. TACE provides a smooth response notably free of withdrawal symptoms.

1. Editorial: Management of the Menopause, J.A.M.A. 158:566 (June 18), 1955. 2. Woodhull, R. B.: Ob. & Gyn. 3:201-3, 1954. 3. Greenblatt, R. S., and Brown, N. H.: Am. J. Ob. Gyn. 6:1361-63, 1952. 4. Edwards, B. E.: J. Indiana St. Med. Assn. 47:869-70, 1954.

Rx Information

TACE

Indications:

Menopause, prostatic carcinoma, postpartum breast engorgement.

Composition:

Each capsule contains 12 mg. of TACE (chlorotrianisene).

Safety:

TACE seldom produces withdrawal bleeding commonly observed following estrogen therapy. In both sexes, TACE is generally well tolerated, minimizing such side effects as nausea, vomiting and fluid retention.

Dosage:

For relief of *menopausal* symptoms, 2 TACE Capsules daily for thirty days, is generally a course of therapy. In severe cases when symptoms recur, additional short courses of TACE may be required. For *postpartum breast engorgement*, 4 TACE Capsules daily for seven days. For palliative control of *prostatic carcinoma*, 1 or 2 TACE Capsules daily.

Supplied:

In bottles of 60 and 300 capsules.

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SORTING OUT CONFUSION

It is announced (*Antibiotic Medicine,* May 1956) that the Upjohn Company and Merck & Co., Inc., have agreed to use the generic name of novobiocin for the antibiotic previously called by them respectively streptonivicin and cathomycin. The two companies will of course continue to use their separate trade names for the substance, which is also prepared under yet a third proprietary name by the Pfizer Company. The three trade names are Albomycin, Cathocin and Cardelmycin respectively.

MEDICINE AND TRAFFIC ACCIDENTS

In West Germany there is considerable concern at the growing number of traffic accidents, and a recent proclamation from the German Medical Association underlines the responsibilities of medical men in this respect. In many German cities there are medical-psychological institutes for traffic safety. The German Medical Association underlines the need for basic research into the qualities which debar a man from driving a vehicle. It appears that in West Germany physical examinations are necessary before a driver is granted his licence. This puts a great responsibility on the doctor who wishes to reject a candidate. He can only do so with authority if the basic research which is part of the traffic safety institute's work has produced sufficient material to guide him in his selection and rejection of candidates on physical and psychological grounds.

RADIOTHERAPY AND SURVIVAL IN BRONCHIAL CARCINOMA

Bignall of London, England, (*Lancet,* 1: 876, 1956) reports a study of 455 patients with bronchial carcinoma, of whom 207 were treated by radiotherapy, and of whom 114 received an estimated tumour dose of up to 3,000 r, and 93 a dose of 4,000 r or more. Their survival was compared with that in 248 receiving no treatment likely to prolong life. The general conclusion from the survey may be summarized as follows: "There seems to be suggestive but by no means conclusive evidence that radiotherapy prolonged the life of some patients in this series; but, even if life were prolonged, it is highly unlikely that the larger doses of radiotherapy given to the most favourable patients – those without manifest mediastinal metastases—caused an increase of as much as 10% in the proportion surviving a year after first attending hospital or 5% in those living for two years.

"This report is not concerned with whether a probable increase of the order suggested justifies greater or less use of radiotherapy in bronchial carcinoma, or with the effects of treatment on the patient's symptoms or his peace of mind."

On the other hand, Smart and Hilton of London, England, (*Lancet,* 1: 880, 1956) point out the advantages of using radiotherapy instead of surgery in a series of selected cases. They selected their cases on the following grounds: The general condition was good, the lesion was localized and so situated that surgery could have been undertaken, and there was no evidence of mediastinal

lymph node involvement. The diagnosis was secured in each case by bronchoscopy and histological section or by positive sputum. They have treated 33 cases by radiotherapy alone over a period of eight years and are satisfied that the results in this small series will bear comparison with those of surgery.

PORPHYRIA

In a recent article in the *South African Medical Journal* (30: 376, 1956) Dr. Dean states that porphyria, a potentially serious familial disorder, is common in South Africa. In Europeans it is inherited as a non-sex-linked Mendelian dominant characteristic and Dr. Dean records a study of 32 porphyric families in which 354 members had clinical manifestations of the disorder. He points out that in the latent stage diagnosis depends on a full personal and family history, with special reference to a history of skin sensitivity, "nervous breakdowns", abdominal pain, operations, pregnancy and drugs that may have been taken. The diagnosis can usually be confirmed in the latent stage by careful examination of the urine and fæces for increased porphyrin excretion. The condition may be aggravated by a wide range of drugs, particularly sedatives such as barbiturates. Sulfonamides are harmful and thiopentone anæsthesia is extremely dangerous. Dr. Dean states that acute attacks of porphyria can usually be dealt with by giving cortisone and placebos. He warns physicians that once a case of porphyria has been diagnosed, the family history must be investigated fully in a search for other affected members. All affected members should be interviewed and should be given a letter stating the evidence on which the diagnosis has been made, mentioning the danger of barbiturates and other drugs; this letter they should show to any doctor they may consult in the future.

Mazingarbe and his colleagues (*Presse méd.*, 64: 627, 1956) draw attention to the fact that porphyria may at times mimic an acute surgical condition. They have collected 18 cases in which an acute porphyria presented abdominal signs for which operation was a possibility. Indeed 12 of these patients had been subjected to exploratory laparotomy. Intestinal obstruction, pancreatitis, and appendicitis may all be simulated by this disease. Operation is of course harmful to the patient and the condition should be thought of in any abdominal syndrome where the clinical signs, the blood picture and the radiology do not appear quite to correspond. Like Dean, Mazingarbe states his belief that porphyria is much commoner than is generally believed.

BURNS AND SCALDS

Two recent articles in the *British Medical Journal* (1: 1379 and 1387, 1956) give a picture of the present position in the United Kingdom as regards burns and scalds. Five years ago, Colebrook and his colleagues from the Burns Research Unit, Birmingham, England, analyzed the records of 2,000 patients admitted to their wards. They now consider what steps have been taken in the interim to prevent burns. In the United Kingdom the main domestic hazard still remains the open fire, either coal, gas or electric. Some progress has been

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made towards fitting proper guards on fires and legislation has been passed making the sale of unguarded new appliances illegal. Some firms are making an effort to produce safer fabrics for clothing for women and children, but there are two possible toxic hazards from materials used to impregnate fabrics, namely, skin dermatitis and the danger of toxicity from ingestion by children sucking their clothes. Broadly speaking, a survey of the present situation shows that it is nearly the same in the United Kingdom as it was ten years ago. There are still over 700 deaths a year from burning accidents and a much larger number of non-fatal but serious burns, many of which entail great suffering and lengthy treatment. Further progress in guarding fires and rendering fabrics less flammable is required.

Tempest, from an injuries centre in Chepstow, Wales, describes a survey of domestic burns and scalds in Wales during 1955. The findings of this survey agree with those of Colebrook in confirming that the vast majority of domestic burns and scalds are preventable. In addition to the measures suggested by Colebrook, Tempest emphasizes the danger arising from overcrowding in houses and from bad design in kitchens, and also advises increased health education on the subject.

INTRAVASCULAR GAS AS SIGN OF FETAL DEATH

Formation of free gas in the circulatory system of the fetus is an early sign of intrauterine death, the largest amounts of gas being found in the umbilical veins and in the heart. It has previously been suggested that the gas develops post mortem, but Christiansen (*Tidsskr. norske laegefor.*, 76: 226, 1956) suggests a different origin. He feels that death of the fetus is in these cases due to a gas embolism in the heart, the gas originating from the maternal blood via the placenta as a result of damage to the latter by Rh immunization.

SIXTH INTERNATIONAL CONGRESS OF OTOLARYNGOLOGY

The scientific program for the plenary sessions of the Sixth International Congress of Otolaryngology, Washington, D.C., May 5-10, 1957, is now complete and includes sessions on chronic suppuration of the temporal bone, collagen disorders of the respiratory tract (in which Dr. Hans Selye of Montreal will participate), and papilloma of the larynx. The deadline for presentation of voluntary papers is October 1, 1956 and applications to present motion-picture films should also be sent in by this date. Information from the General Secretary, 700 North Michigan Avenue, Chicago 11, Illinois.

COUGH SYNCOPE

Until recently it has been thought that fainting following close on a

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paroxysm of uncontrollable coughing was a rare syndrome, but recent studies have suggested that it is a common form of fainting. The patient usually recovers rapidly from his loss of consciousness, which may take place within three to five seconds of the onset of his cough. Studies by McIntosh and his colleagues (*Am. Heart J.*, 52: 70, 1956) on subjects with cough syncope and on normal subjects suggest to them the following explanation for the phenomenon. They suggest that a sudden great increase in intrathoracic and intra-abdominal pressure may lead to a rise in cerebrospinal fluid pressure; this in turn squeezes the blood out of the brain and leads to fainting.

PARTHENOGENESIS IN HUMAN BEINGS

It has recently been suggested that parthenogenesis or procreation without sexual union is a possibility in human beings and that this event could be recognized by certain criteria. A mass-circulation newspaper in Britain started an enquiry whether there were any mothers in the country who genuinely believed that they had given birth to a parthenogenetic child. Nineteen claimants presented themselves and their claims were scientifically investigated by some London physicians. A preliminary interview sufficed to eliminate 11 of the pairs of mothers and daughters. Blood group studies were carried out on the remaining eight pairs. In four pairs, differences in blood antigens eliminated them from the study, and of the other four one pair were eliminated on the colour of their eyes (the mother had blue eyes and the daughter had brown eyes). Additional tests were then carried out, including tests for tasting of phenyl thiocarbamide, tests for secretors and direct filter-paper serum electrophoresis. Finally in the one pair which had not been eliminated skin-grafting from mother and child were performed, and the grafts were found incompatible. It is claimed that this final mother's claim must not only be considered seriously, but that it has not so far been disproved.—*Lancet*, 1: 1072, 1956.

CIBA FOUNDATION

The 1955 Report of the Ciba Foundation for the Promotion of International Co-operation in Medical and Chemical Research is to hand. This Foundation, which has its headquarters in London, England, provided accommodation during 1955 for nearly 800 visitors from 30 different countries, while they spent short periods in London in connection with their scientific work. A new conference room and an attractive library have been added to headquarters. The activities of the Foundation include informal discussion meetings, 45 of which have been held within the last 12 months, a quarterly clinical forum in which 20 to 30 people engaged in related practice or research exchange their views, film sessions, and Ciba Foundation con-

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ferences. There have now been 37 of the latter, which are small, moderately informal conferences on various aspects of medical and clinical research, confined to 30 participants and with proceedings in the English language alone. The 1955 list includes conferences on porphyrin biosynthesis and metabolism, histamine, extrasensory perception, the nature and actions of the internal secretions of the pancreas, aging in transient tissues, bone structure and metabolism, and paper electrophoresis. Professor Olivecrona, Professor of Neurosurgery in Stockholm, gave the annual Ciba Foundation lecture on hypophysectomy in diabetes, with Professor C. H. Best of Toronto in the chair. In addition, the first awards in support of research relevant to problems of aging have been made.

SERUM PROTEINS AND PULMONARY TUBERCULOSIS

It is suggested as a result of studies on 327 adult patients with pulmonary tuberculosis that study of the serum proteins may yield an index of activity. It was found that with increased activity and extent of the disease, the albumin concentration in the serum fell and the alpha-2 globulin concentration rose progressively. Conversely these fractions were returned towards normal as the disease became arrested, or during treatment with antituberculosis drugs. The ratio of albumin to alpha-2 globulin should provide a useful objective index of activity.—Gilliland *et al.*: *Brit. M. J.*, 1: 1460, 1956.

NEUROPSYCHIATRIC CONSEQUENCES OF PREMATURITY

In Baltimore a group of 500 premature infants and a matched group of 492 full-term control infants were observed by Gesell developmental examination and physical examination at the age of 40 weeks, and at the corresponding corrected age for premature infants. It was found that the incidence of abnormality increases as the birth-weight group of the infant decreases. Of the premature infants, 8.2% had some serious neurological abnormality (possible cerebral palsy plus overt neurological defect), whereas the controls showed a rate of only 1.6%. In the case of mental deficiency, the difference between the two groups was not statistically significant (2.6% and 1.6% respectively). Of the infants with a birth-weight less than 1,501 g., one-half had a neurological or intellectual defect, and some also had a major visual handicap.—Knobloch *et al.*: *J. A. M. A.*, 161: 581, 1956.

BIRTHDAY HONOURS

Two former presidents of the British Medical Association were specially honoured in the Birthday Honours List issued this June. Sir Henry Cohen, the well-known Liverpool physician and chairman of innumerable committees on medical matters, has been raised to the peerage, where he will undoubtedly play a great part in interpreting medical matters to his fellow peers. Mr. Tudor Thomas, of Cardiff, the well-known eye surgeon whose name is particularly associated with corneal grafting, has been knighted.

AMERICAN BOARD OF OBSTETRICS AND GYNECOLOGY

Following the annual meeting and completion of the Part II Examinations of the American Board of Obstetrics and Gynecology, the following statistics were compiled:

Out of the total number of 471 new and reopened applications this year, 108 were postponed by the Credentials Committee. Of 430 candidates who took the Part I Examinations, there were 48 failures; 25 were failures in the Written Examinations and 23 in Case Reports. There were a total of 415 candidates who participated in the Part II Examinations; 317 were certified and 99 failed.

Applications for certification for the 1957 examinations are now being accepted. All candidates are urged to make such application at the earliest date possible. Deadline date for receipt of applications, new and reopened, is October 1.

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ACHROMYCIN

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Current bulletins outlining present requirements may be obtained by writing to the Secretary's office: Robert L. Faulkner, M.D., American Board of Obstetrics and Gynecology, 2105 Adelbert Road, Cleveland 6, Ohio.

RECENT ADVANCES IN CLINICAL PRACTICE

The University of Buffalo School of Medicine announces a general and comprehensive postgraduate course for practitioners, which will review recent advances in diagnosis and therapy. The course will be held from Monday, September 10, to Saturday, September 15, and will take place at a different hospital in Buffalo each day. The fee for the course is $75. Information from: Dr. Milton Terris, University of Buffalo School of Medicine, 3435 Main Street, Buffalo 14, New York.

HOSPITAL STATISTICS

The American College of Surgeons, American Hospital Association, American College of Physicians and the Southwestern Michigan Hospital Council anounce the joint organization of a new Commission on Professional and Hospital Activities. This Commission has been established to conduct a medical statistical service which will help hospitals to simplify their medical records and to analyze their records more effectively than has been done in the past.

The Kellogg Foundation has given a substantial grant in support of this program for three years, after which it is expected that this service will be self-sustained. The program will permit mechanization of tabulation and indexing of hospital statistics and will therefore enable hospitals to obtain more complete and reliable data on the job of medical care which they are doing.

This Commission is an extension of the Study on Professional Activity which has been carried on for the last three years by the Southwestern Michigan Hospital Council. This study, in which 23 member hospitals participated, demonstrated the development of a simplified method of collecting and reporting medical statistics for hospitals. Experience in Michigan indicated that service could be furnished at a cost within the reach of even the small community hospitals, and that mechanization of medical statistical procedures could actually save hospitals money.

COURSE IN PHYSICAL MEDICINE AND REHABILITATION

The University of Buffalo School of Medicine announces an extensive course in physical medicine and rehabilitation, planned to give the physician an understanding of techniques employed in this field. The course is limited to five physicians and will take place on 20 Wednesdays beginning September 26, 1956. Information from Milton Terris, M.D., Assistant Dean for Postgraduate Education, University of Buffalo School of Medicine, 3435 Main Street, Buffalo 14, New York.

SUICIDE AND NEUROPLEGICS

Gosselin and Gervais have examined the statistics for suicide from 1906 onwards for inpatients treated at the St. Michael Archangel Hospital, Quebec. They find that during the last year, during which there has been an intensive employment of neuroplegic drugs in the hospital, there have been no less than six cases of suicide, a rate of six per thousand, which compares very unfavourably with the previous rate of approximately 0.9 per thousand. The authors admit that this could be a coincidence, but find it disturbing and wonder whether more frequent suicide will become a problem of neuroplegic therapy. — *Laval méd.*, 21: 784, 1956.

UROLOGY AWARD

The American Urological Association offers an annual award of $1,000 (first prize of $500, second prize $300 and third prize $200) for essays on the result of some clinical or laboratory research in urology. Competition will be limited to urologists who have been graduated not more than ten years, and to hospital interns and residents doing research work in urology. The first prize essay will appear on the program of the forthcoming meeting of the American Urological Association, to be held

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at the Hotel William Penn, Pittsburgh, Pennsylvania, May 6-9, 1957.

For full particulars write the Executive Secretary, William P. Didusch, 1120 North Charles Street, Baltimore, Maryland. Essays must be in his hands before December 1, 1956.

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LARYNGOLOGY COURSE

The next laryngology and bronchoesophagology course to be given by the University of Illinois, College of Medicine, is scheduled for November 5-17, 1956. The course is under the direction of Dr. Paul H. Holinger.

Interested registrants will please write directly to the Department of Otolaryngology, University of Illinois, College of Medicine, 1853 W. Polk Street, Chicago 12, Ill.

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MODE OF ACTION OF RESERPINE

Further work from the Laboratory of Chemical Pharmacology at the National Institutes of Health, Bethesda, Maryland, strengthens the belief that reserpine and other tranquillizing rauwolfia alkaloids act upon the brain by an indirect effect on serotonin (5-hydroxytryptamine), a substance normally present in the brain. In experiments on rabbits, the serotonin concentration in the rabbit brain was found to fall very significantly after administration of rauwolfia alkaloids. On the other hand, related alkaloids which had no sedative action also had no effect on brain serotonin. It is interesting to note that chlorpromazine failed to release serotonin from its depots, in spite of its tranquillizing effect. It is presumed that the central action of chlorpromazine is not mediated through the release of serotonin.—*Science*, 123: 992, 1956.

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THE SIGNIFICANCE OF MICROHÆMATURIA

When examination of the urine discloses the presence of red blood cells in a patient without symptoms of urological disease, what should be done? Greene and his colleagues from the Mayo Clinic (*J. A. M. A.*, 161: 610, 1956) have studied 500 cases in which red cells were present in the urine of patients without symptoms. They find that further urological study led to the discovery of a significant abnormal finding in about 10% of patients; the lesion was neoplastic in about 2%. The remaining 90% of patients could be divided into approximately equal groups in which no lesion was detected or in which a lesion was insignificant. The authors attempted to establish criteria for separating off the significant cases from the rest, but failed to do so. They therefore recommend that the finding of red cells in the urine be the signal to perform a complete urological investigation in all patients over 50 years of age, but that a modified plan consisting of taking a plain radiograph of the urinary tract together with cystoscopy be carried out in younger patients.

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INTERNATIONAL COLLEGE OF SURGEONS

The 21st Annual Congress of the United States and Canadian Sections, International College of Surgeons, will be held in the Palmer House, Chicago, September 9-13.

The International House of Delegates also will meet on the morning of the opening day, Sunday. In the afternoon, the House of Delegates of the United States Section will convene for the biannual election of officers and for other business. General assemblies will be held mornings and afternoons, Monday through Thursday. Section meetings at the same hours will cover coloproctologic surgery, neurosurgery, obstetrics and gynæcologic surgery, occupational surgery, ophthalmology and otorhinolaryngology, orthopædic surgery, plastic surgery, rehabilitation services, surgical nurses and urologic surgery. A film forum will be presented on Monday evening. All-day scientific motion picture programs will be given Monday through Thursday. The annual banquet will be on Wednesday evening. The annual convocation will take place in the Civic Opera House on Thursday evening.

The Canadian Section will hold a business meeting Monday afternoon and its dinner will be given that evening.

Further information may be had by writing to the Secretariat, In-

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ternational College of Surgeons, 1516 Lake Shore Drive, Chicago 10, Illinois.

FEDERAL HEALTH GRANTS

British Columbia. — Three new federal health grants for mental health research at the University of British Columbia and one for hospital construction in Victoria have been awarded. At the University of British Columbia a grant of $13,577 will be used for research in metabolism of the body during schizophrenia. The project will be carried out under the direction of Dr. W. C. Gibson, professor of neurological research, University of British Columbia, and is expected to take from two to three years. A grant to the University of British Columbia of $12,271 will be used for research into effect of methods of treatment in mental disease on the structure of the brain. A third grant to U.B.C., one for $8,673, will be used for a survey of the causative factors in mental deficiency and will be carried out at the Woodlands School, New Westminster. It is hoped that the survey will pinpoint future needs in the field of mental deficiency and assist with the problems of classification and rehabilitation of mentally deficient persons. Both of these projects will be carried out under the direction of Dr. W. C. Gibson.

In Victoria a grant of $10,500 goes to the Royal Jubilee Hospital to assist in financing the cost of an addition to their psychiatric unit.

New research projects dealing with various aspects of child and maternal health in British Columbia are also to get federal assistance. A grant of $7,488 goes to the British Columbia Medical Research Institute for a study of the incidence and the relationships of the various factors responsible for staphylococcal infections. The study will be carried out at the Research Institute under Dr. A. F. Hardyment of the Pædiatrics Department, Vancouver General Hospital.

A grant of $2,100 has been awarded to the University of British Columbia for studies on the morbidity of both mother and fetus during pregnancy. The project will be undertaken by Dr. Alec M. Agnew, head of the department of obstetrics and gynæcology, U.B.C. In the course of the project a detailed study of maternal deaths will be made to assess the circumstances surrounding them and to assess whether deaths could be classified as preventable or otherwise. The research will be carried out in close collaboration with the department of public health, U.B.C., the provincial health department and the committee on maternal welfare of the B.C. Division of the Canadian Medical Association.

A grant of $6,000 will be used for research in the blood levels of adrenal gland steroids and their effect on resistance to disease. The results of the study, to be undertaken by Dr. F. E. Bryans, department of obstetrics and gynæcology, U.B.C., are expected to help in reducing the prenatal fetal mortality rate.

Alberta.—Federal health grants totalling $144,000 have just been awarded to Alberta to assist in ex-

pansion plans of Rosehaven Hospital, Camrose.

A grant of $75,000 goes towards construction costs of a new frame and stucco building to provide additional accommodation for patients. The new building will house two wings of 25 beds each, with a dining room, day rooms and other facilities.

A second grant, for $69,000, will go towards the costs of a new dormitory addition to the provincially owned hospital with accommodation for 46 patients and related facilities.

Ontario.—New national health grants totalling more than $290,000 for hospital construction projects will assist in providing Ontario with additional hospital beds, nurses' accommodations, community health centres and other facilities.

The largest grant of $116,456 goes to Humber Memorial Hospital, Weston. The grant will contribute to the establishment of 64 additional active treatment beds, 10 recovery and seven labour beds, 40 bassinets, 6,637 square feet of floor space for community health centre facilities and generally to improvement in the hospital's medical, surgical and obstetrical services. New construction calls for the change of a nursery into pædiatric wards, the establishment of a laboratory from the former x-ray department and an enlarged surgical suite in what was formerly a delivery suite.

Almost as large a federal grant goes to the Sydenham District Hospital, Wallaceburg, with approval of $94,450 towards construction to give that institution 77 new active treatment beds, two labour beds, 24 bassinets and outpatient facilities.

Grants of $24,000 go to the Queensway General Hospital, Toronto, to assist in construction of a nurses' residence with accommodation for 48 nurses; $22,800 to St. Joseph's Hospital, London, to make space available for outpatient facilities; $10,160 to the Civic Hospital, Ottawa, to enable the hospital to provide space for outpatient services, including an addition to the radioisotope laboratory and cobalt therapy unit; $9,000 to the Royal Victoria Hospital, Barrie, to provide space for 18 nurses' beds; $6,000 to assist in establishing 12 nurses' beds at the Haldimand War Memorial Hospital, Dunnville; $4,273 to St. Joseph's Hospital, Hamilton, to assist with the cost of alterations for a new physiotherapy department, and $3,125 to St. Vincent's Hospital, Ottawa, to provide additional accommodation for 10 nurses.

JOHN RYLE MEMORIAL PRIZE

The Medical Association for the Prevention of War is offering a prize of £75 to be called the John Ryle Memorial Prize for the best essay under the title "A World Approach to Human Survival and Health". It will be recalled that Dr. John Ryle was originally a physician on the staff of Guy's Hospital, London, England, and subsequently Regius Professor of Physic at Cambridge and Professor of Social Medicine at Oxford. Information about the prize is obtainable from Dr. D. L. Kerr, 291 Burntwood Lane, London, S.W.17, England.

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Riboflavin	1.25	mg.
Niacinamide	7.5	mg.
Vitamin B_{12} (crystalline)	2.5	mcg.
Folic acid	0.25	mg.
Ascorbic acid (from sodium ascorbate)	75	mg.
Pyridoxine hydrochloride	0.75	mg.
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